BRITISH MEDICAL JOURNAL

LONDON SATURDAY MAY 24 1958

SUPPURATIVE ARTHRITIS COMPLICATING RHEUMATOID ARTHRITIS

BY

J. H. KELLGREN, M.Sc., F.R.C.P., F.R.C.S.

J. BALL, M.D., B.Sc. R. W. FAIRBROTHER, T.D., M.D., D.Sc., F.R.C.P.

AND

K. L. BARNES, F.R.C.S.

Rheumatism Research Centre, University of Manchester, and Departments of Clinical Pathology and Orthopaedic Surgery, Manchester Royal Infirmary

In recent years we have observed 12 patients with rheumatoid arthritis who developed severe and sometimes fatal bacterial infection in connective-tissue structures. In nine cases this was mainly a suppurative arthritis, which was often polyarticular; in two cases the infection was mainly in the bones; and in the remaining case there were multiple subcutaneous and muscular abscesses. This complication of rheumatoid arthritis is therefore not uncommon, and since it presents some diagnostic and therapeutic problems and is a grave threat to life it seemed desirable to report our experience with these patients in some detail, especially as we have been unable to find any previous report of a similar series. Coste *et al.* (1957), however, reported a case of polyarthritis complicated by two episodes of staphylococcal septicaemia, and Bywaters (1953) mentions the occurrence of staphylococcal arthritis in patients with rheumatoid arthritis in discussing two cases of what he calls fistulous rheumatism.

In some of our earlier cases the extent of suppuration was revealed only by a systematic examination of the joints at necropsy; but with increasing experience and awareness of the problem we have been able to make a correct diagnosis at an earlier stage and reduce mortality by appropriate treatment.

In two patients the infecting organism was a coliform bacillus, but in the other ten it was a staphylococcus, and in all but three of these the staphylococcus was resistant to penicillin.

The cases are described in chronological order and their main features are summarized in Tables I and II.

Case 1

A retired business man aged 63 was admitted to the infirmary in July, 1950, for severe progressive rheumatoid arthritis of five years' duration. During the six months before admission he had been constitutionally ill and had lost 20 lb. (9 kg.) in weight, and during the last two weeks he developed an unproductive cough.

On admission he was obviously ill, with a fever up to 101° F. (38.3° C.). He had a severe inflammatory erosive arthritis of all the limb joints, some limitation of spinal movement, numerous subcutaneous nodules, lymphadenopathy, and a large left pleural effusion. E.S.R. 106 mm. (Westergren), Hb 12.0 g./100 ml., W.B.C. 9,000, sheep-cell agglutinating titre (S.C.A.T.) 512, serum albumin 3.6 g./100 ml., serum globulin 3.5 g./100 ml. The pleural fluid was blood-stained but sterile on culture; bronchoscopy and

TABLE II

Case No.	Corticosteroids or Corticotrophin Before Infection	Range of S.C.A.T.	Serum Proteins (g. 100 ml.)		Range of W.B.C.
			Alb.	Glob.	
1	Corticotrophin 2 wks	256–64–2048	3·6	3·5	4,000–13,000
2	None	—	1·7	4·1	5,000–16,900
3	,,	512–1024	3·2	2·5	4,000– 5,800
4	Cortisone, 100–25 mg.	256–4–64	4·0	2·3*	4,400–18,000
5	None	512	3·1	2·8	3,500– 5,200
6	Cortisone, 75 mg.	—	2·8	2·6	9,000–24,000
7	None	—	—	—	4,200– 4,800
8	,,	64–512	2·6	3·2	4,900–13,400
9	,,	256–8–32	2·1	2·9	5,000–22,000
10	,,	8	2·9	3·9*	6,700–10,200
11	Prednisolone 20–30 mg.; corticotrophin	256–2048	1·8	4·3*	6,000–11,000
12	None	256	2·4	3·0*	10,000–22,000

* Electrophoresis done.

TABLE I.—*Details of Patients with Suppurative Complications of Rheumatoid Arthritis*

Case No.	Sex and Age	Rheumatoid Arthritis			Infection		
		Severity	Duration	Nodules	Sites	Organism	Outcome
1	M 63	Severe	5 yrs	++	Hallux, pleura, knees, subacromial bursa, blood, biopsy wound	*Staph. aureus*	Recovered
2	M 41	,,	4 ,,	+++	Wrists, elbows, shoulder, sternoclavicular, blood	,, ,,	Died
3	F 49	,,	12 ,,	++	Knees, subacromial bursa, elbow	,, ,,	Recovered
4	F 47	,,	18 ,,	++	Ribs, cervical vertebra, sacrum	,, ,,	Died
5	F 66	,,	7 ,,	+++	Shoulder-joint, blood, urinary tract	Coliform	,,
6	M 45	,,	1½ ,,	+++	Knees, wrist, sternoclavicular, urinary tract	,,	,,
7	M 54	Moderate	3 ,,	+	Tarsus, wrist, metacarpo-phalangeal, olecranon bursa, blood, lungs, tricuspid valve	*Staph. aureus*	,,
8	F 56	Severe	20 ,,	+	Hip, ilium, chest wall	,, ,,	Recovered
9	M 51	Moderate	5 ,,	—	Ankle, elbows, knees, shoulder, blood	,, ,,	,,
10	F 37	Doubtful	6 mths	0	Multiple muscular and subcutaneous abscesses	,, ,,	,,
11	M 39	Severe	13 ,,	++	Saphenous vein, blood, chest wall, knee, wrist, elbow, metatarso-phalangeal, interphalangeal	,, ,,	,,
12	M 60	,,	20 yrs	+++	Ribs, blood, knee	,, ,,	,,

examinations for tubercle bacilli were negative. During August he was given a three-weeks course of corticotrophin, which produced severe hypercortisonism and striking amelioration of the arthritis and improvement in his general health. Biopsies of elbow nodules were performed before and during the course of corticotrophin.

In September, after withdrawal of the corticotrophin, his condition had deteriorated again and irregular pyrexia up to 100° F. (37.8° C.) recurred. The biopsy wound on the right elbow remained unhealed. The pleural effusion increased and a painful swelling appeared over the right first metatarsophalangeal joint; this discharged pus, revealing a sinus down to the joint. Cultures from this sinus, the elbow wound, and pleural fluid all grew a *Staph. aureus* sensitive to penicillin, but blood culture was sterile. He improved on a course of penicillin and remained afebrile throughout October, though his rheumatoid arthritis remained active.

During the first week of November fever returned, became remitting up to 104° F. (40° C.) with rigors, and he was desperately ill. The left shoulder became painful, and on November 12 pus was aspirated from the left subacromial bursa. This pus, and blood taken three days previously, grew a *Staph. aureus* resistant to penicillin and streptomycin but sensitive to other available antibiotics, and a few days later a similar organism was grown from pus aspirated from the right knee and the left pleura. He was treated with chlortetracycline and penicillin, and repeated aspiration of infected joints and pleura. Finally the subacromial bursa and the empyema were drained surgically and he eventually made a good recovery, leaving hospital walking well in April, 1951, with his arthritis in fair remission and all wounds healed.

Numerous white-cell counts were done throughout his stay in hospital. These ranged from 4,000 to 10,000 in spite of the widespread suppuration, and only on one occasion, when he had pyrexia and rigors, did the count rise to 13,000.

Case 2

A man aged 41 had developed progressive rheumatoid arthritis in 1945 while on military service. In September, 1949, he was admitted to Withington Hospital under the care of Dr. H. S. Barber.

On admission he was bedridden with a very severe inflammatory polyarthritis affecting all the limb joints. Nodules were present on the elbows and elsewhere. He was ill, emaciated, had pyrexia up to 100° F. (37.8° C.), and there was lymphadenopathy but no other evidence of visceral disease. E.S.R. 118 mm. (Westergren), Hb 9.1 g./100 ml., W.B.C. 5,200, serum albumin 1.7 g./100 ml., globulin 4.1 g./100 ml. Nodules over the sacrum ulcerated, but otherwise his condition remained unchanged until February, 1950, when the fever became remittent, rising to 103° F. (39.4° C.), and his general condition deteriorated.

He was given penicillin without effect, and an abscess appeared on the right wrist. This was drained on February 20 and the pus grew a staphylococcus resistant to penicillin but sensitive to streptomycin and chlortetracycline. He was given chlortetracycline and streptomycin, but he continued to deteriorate. An abscess which appeared over the left wrist was incised. This grew a similar staphylococcus, and the same organism was obtained from a blood culture. Later both elbows, the right shoulder, and the left sternoclavicular joint became more painful and swollen, and on March 4 pus was drained from the shoulder. His general condition deteriorated rapidly, however, and he died on March 9, about four weeks after the presumed onset of joint infection. The white-cell count on admission was 5,200, and it remained under 8,000 throughout the illness except for one count of 16,900 at the time of the first wrist abscess.

Necropsy disclosed widespread severe rheumatoid arthritis and pyarthrosis of both wrists, right shoulder, and left sternoclavicular joint, with a large chest-wall abscess arising from this. Pus from this abscess produced a pure culture of a staphylococcus similar to the one grown previously from abscesses. The sternoclavicular joint was lined by necrotic tissue densely infiltrated with polymorphs. The spleen was enlarged, with a doubtful increase of polymorphs in the red pulp. The remaining viscera were not remarkable.

Case 3

A housewife aged 49 was admitted to the infirmary on January 19, 1952, with a 12-years history of progressive rheumatoid arthritis. For some months prior to admission her condition had deteriorated, and three days before admission the right shoulder and left knee had become very painful. On examination she presented the picture of a severe destructive polyarthritis of the mutilans type affecting mainly the hands, feet, and cervical spine. There were numerous subcutaneous nodules, some of which were ulcerated and appeared infected. The right shoulder and left knee were warm, swollen, and more painful than the other joints. There was lymphadenopathy and the spleen was just palpable, but no other evidence of visceral disease was found.

She remained afebrile; the white-cell count was 4,300, but the E.S.R. was 123 mm. (Westergren) and Hb 9.2 g./100 ml., S.C.A.T. 512, serum albumin 3.2 g./100 ml., globulin 2.5 g./100 ml. The shoulder and knees became more swollen and painful, and on January 31 aspiration was performed, and to our great surprise pus was obtained from the left knee and right subacromial bursa. Similar pus was also obtained from the right elbow. Cultures of all three specimens grew a *Staph. aureus* sensitive to penicillin, but blood culture was sterile. Penicillin was given both locally and parenterally (1 mega unit six-hourly). The shoulder and knee were drained the next day. Progress seemed satisfactory, but the knee remained painful with a discharging sinus, and *Pseudomonas pyocyanea* was cultured from the sinus on February 18. The knee was immobilized in plaster and the patient returned home. The highest white-cell count recorded was 5,800, and she remained afebrile through the whole illness. Although recurrent abscesses formed around the knee, bony ankylosis was finally achieved, and she continued to live an active life and run her home until October, 1957, when she developed a sudden partial tetraplegia from a cervical subluxation and was admitted to hospital again for reduction of the subluxation and spinal fusion.

Case 4

A housewife aged 47 was admitted to the infirmary on October 14, 1952, with a severe progressive rheumatoid arthritis of 18 years' duration. During the six months prior to admission there had been a severe exacerbation of her disease and she had become bedridden. On examination she was constitutionally ill and crippled by a severe destructive erosive polyarthritis of all the limb joints and spine. There were numerous nodules over elbows, occiput, and spine; the right eye showed keratoscleritis; there was lymphadenopathy but no other evidence of visceral disease. E.S.R. 70 mm. (Westergren), Hb 8.5 g./100 ml., W.B.C. 4,400, S.C.A.T. 256, serum albumin 4 g./100 ml., globulin 2.3 g./100 ml. A course of gold was given without effect, and in November cortisone, 100 mg. daily, was started. This also had little effect, and the cortisone was gradually withdrawn after two months. Towards the end of December she became increasingly ill, with pyrexia up to 100° F. (37.8° C.), and developed coryza and a dry cough. On December 30 she had a rigor and started to cough up purulent sputum. Moist sounds were heard over the bases of both lungs. Blood culture on December 31 remained sterile, and the sputum which was cultured on many occasions grew only normal upper respiratory flora. She was given penicillin and later chlortetracycline. By the end of January, 1953, the fever subsided, but her general condition was unsatisfactory and the arthritis remained very active.

In March remitting pyrexia returned, rising to 104° F. (40° C.) with rigors; purulent sputum increased, but blood

culture on March 5 remained sterile and the sputum still grew only normal flora. On March 11 an abscess appeared over the sacrum. This was drained and the pus grew a *Staph. aureus* resistant to penicillin and streptomycin but sensitive to other available antibiotics. She was given chloramphenicol, 0.25 g. four-hourly, without effect, and died on March 20. *X*-ray examination of the chest on admission was normal. During the two periods of severe illness chest films showed patchy opacities at both bases consistent with bronchopneumonia. At the end of January numerous fractures of osteoporotic ribs were noted; these were thought to be cough fractures at the time. Throughout her illness the white-cell count remained below 10,000, except for one count of 12,000 in February and a terminal count of 18,000 ten days before her death.

At necropsy several of the numerous rib fractures were ununited, and these were the site of small abscesses, pus from one of which yielded a heavy growth of *Staph. aureus* resistant to penicillin and streptomycin but sensitive to other available antibiotics. In addition, microscopical examination revealed extensive focal abscess formation in the medulla of the ribs and in the bodies of the cervical vertebrae. There were also a severe rheumatoid arthritis, a chronic gastric ulcer, perisplenitis, and a mild bronchopneumonia of the left lower lobe. Apart from some degranulation of pituitary basophils and a probable increase in the number of polymorphs in the spleen, no significant changes were noted in the viscera histologically.

Case 5

A housewife aged 66 was admitted to the infirmary on December 10, 1952, under the care of Professor Robert Platt. For seven years she had had a severe progressive rheumatoid arthritis, and during the three months before admission there had been a deterioration in general health as well as in the joint condition.

On admission she was ill but afebrile. There was a severe inflammatory erosive arthritis of all the limb joints and the upper spine. Nodules were seen on the elbows and in the sclera of the right eye. There was lymphadenopathy, the liver and spleen were slightly enlarged, and the left kidney was palpable, but there was no albuminuria. E.S.R. 52 mm. (Wintrobe), Hb 10.5 g./100 ml., W.B.C. 3,500, S.C.A.T. 512, serum albumin 3.1 g./100 ml., globulin 2.8 g./100 ml. Congo-red test showed no evidence of amyloid; thymol turbidity 11 units, serum alkaline phosphatase 22 units. An intravenous pyelogram revealed a non-functioning right kidney but good excretion in the left. She was treated with bed rest and aspirin, and hydrocortisone drops were instilled in the right eye. Her condition improved slightly, and on December 20 she was transferred to the Devonshire Royal Hospital, Buxton.

Her progress seemed satisfactory until the evening of December 31, when she had a fever of 100° F. (37.8° C.) and spent the night muttering confusedly. The next morning she was afebrile and lucid, but during the following days she developed slight diarrhoea, became increasingly lethargic, lost her appetite, and had occasional chills and slight pyrexia. On January 24, 1953, she had a rigor and fever of 102° F. (38.9° C.), and the following day she was readmitted to one of the rheumatism beds of the infirmary. She was now seriously ill and lethargic but afebrile, and the physical findings were the same as on her previous admission except that the left eye and the right shoulder were more painful. W.B.C. 5,100; no L.E. cells could be found; blood urea 48 mg./100 ml. After five days fever reappeared, and blood culture on February 2 grew a coliform bacillus resistant to penicillin and streptomycin but sensitive to chloramphenicol. The urinary sediment contained only a few epithelial and pus cells but many Gram-negative rods, and culture produced a profuse growth of coliform bacilli. Swabs from the right eye were sterile. A course of chloramphenicol was given without effect, and she died on February 13.

Necropsy showed severe destructive nodular rheumatoid arthritis and pyarthrosis of the right shoulder, from which coliform bacilli were obtained in pure culture. The infected joint was lined by a necrotic layer infiltrated with polymorphs; in the deeper parts of the joint capsule multinucleate giant cells (an exceptional finding in uncomplicated rheumatoid arthritis) were scattered among dense collections of plasma cells and lymphocytes. There was an active but chronic pyelonephritis in the hypoplastic right kidney, and a recent pyelonephritis of the left kidney. Apart from non-specific splenic capsulitis and degranulation of pituitary basophils, the remaining viscera showed nothing of note. The vertebral marrow was within normal limits.

Case 6

A male labourer aged 44 was admitted to Withington Hospital on September 25, 1953, under the care of Dr. H. S. Barber. He gave a nine-months history of pain and swelling of the limb joints with malaise and a weight loss of 20 lb. (9 kg.).

On examination he was ill, with a pyrexia of 101° F. (38.3° C.). He had a symmetrical inflammatory polyarthritis of all limb joints and cervical spine, but there was no evidence of visceral disease. E.S.R. 75 mm. (Westergren), Hb 12 g./100 ml., W.B.C. 11,000. After a few weeks the fever disappeared and he was transferred to the Devonshire Hospital, Buxton, for long-term conservative treatment with bed rest, splintage, aspirin, and gold. His condition deteriorated steadily and he developed numerous ulcerating nodules. Throughout this period he had some cough with purulent sputum, but chest films revealed only indefinite signs of bronchopneumonia, and no tubercle bacilli or other pathogenic organisms could be recovered from the sputum. He also had several attacks of mild diarrhoea. Many tests for L.E. cells were all negative.

In June, 1954, he was started on cortisone, 75 mg. daily, but this had little effect, and the dosage was gradually reduced to nil during October. On October 20 he was readmitted to Withington Hospital because of persistent fever and continued deterioration of his polyarthritis. E.S.R. 140 mm. (Westergren), Hb 8.4 g./100 ml., W.B.C. 17,000, serum albumin 2.8 g./100 ml., globulin 2.6 g./100 ml. On November 1 coliform bacilli were cultured from the urine, which contained numerous red cells but no pus cells or casts. During the second week of November he had several rigors and an irregular remitting fever up to 103° F. (39.4° C.), but blood culture remained sterile. He had been given courses of penicillin and chlortetracycline without effect, and he died on November 22.

Necropsy showed severe nodular rheumatoid arthritis and pyarthrosis of both knees, right wrist, and sternoclavicular joint. Pus from the right knee-joint contained numerous Gram-negative bacilli, and culture yielded a coliform organism sensitive to all available antibiotics except penicillin. The thickened synovial tissues of the joint showed an inner necrotic layer densely infiltrated with polymorphs and an outer zone densely infiltrated with plasma cells and lymphocytes, among which were scattered multinucleate giant cells and small groups of foam cells. Numerous focal microscopic abscesses were found in the marrow of the sternum. There was also non-specific perisplenitis and a gastric ulcer. Gram-negative bacilli were found in the sinusoids of the liver and in the small blood vessels of the kidney and adrenal, but there were no visceral abscesses.

Case 7

A male secretary aged 54 was admitted to the infirmary as an emergency case on October 8, 1953. His polyarthritis had begun three years previously and he had been seen in the rheumatism clinic in May, 1952, at which time he had an inflammatory polyarthritis affecting the hands, feet, and elbows, with nodules over the elbows and in the long flexor tendons of the fingers. There were no signs of visceral disease. E.S.R. 36 mm. (Westergren), W.B.C. 6,400,

Hb 14.5 g./100 ml. He was considered to have typical rheumatoid arthritis of moderate severity, and his doctor was advised to treat him with soluble aspirin and a course of gold. Following this he improved, and continued at work until 14 days before admission, when there was a sudden onset of malaise, rigors, and intermittent fever. He had had much malaria during his war service, and his doctor thought this might have recurred, but treatment with quinine was ineffective. After a few days he developed acutely painful red swellings over several joints, and salicylates and colchicine were given. Diarrhoea followed, and this persisted after the colchicine was discontinued. His fever remained high, and two days before admission an erythematous rash appeared over face and trunk.

On admission he was gravely ill, with a fever of 101° F. (38.3° C.). He was dyspnoeic and weak; there were signs of basal bronchopneumonia, the abdomen was distended, and the lymph nodes were slightly enlarged. There was a grade 2 systolic cardiac murmur. The urine contained both sugar and albumin. He had a very acute inflammatory arthritis of the left tarsus and carpus and the third metacarpo-phalangeal joint of the right hand. The left olecranon bursa was also inflamed. The remaining joints of the hands and feet showed only slight thickening and limitation of motion. W.B.C. 4,200, Hb 12 g./100 ml., blood urea 150 mg./100 ml. Blood culture taken on admission grew *Staph. aureus* (1,000/ml.) sensitive to penicillin and other available antibiotics. He was given penicillin, 1 mega unit four-hourly. Later chlortetracycline was added, and 400 mg. of cortisone given intramuscularly and 100 mg. of hydrocortisone and chlortetracycline given by intravenous drip, but his condition deteriorated rapidly and he died five days after admission.

Necropsy revealed a bacterial endocarditis superimposed on a fibrinoid necrotic lesion of the tricuspid valve and septic infarcts of the lungs. The left olecranon bursa was distended with pus, which yielded a pure growth of *Staph. aureus* similar in sensitivity to that recovered from the blood. There was also a pyarthrosis of the radio-carpal joint and the third carpo-metacarpal joint; and a large abscess cavity was found in the deep subcutaneous tissues of the palm which communicated with the third metacarpo-phalangeal joint. Focal abscesses were present in the fatty marrow in the juxta-articular regions of the third metacarpal and the lower end of the radius. Histologically the infected joints were lined by a necrotic membrane densely infiltrated with polymorphs. The spleen was enlarged and soft, but there was no increase in the number of polymorphs in the red pulp. No other significant findings were encountered in the viscera. The sternal marrow appeared to be normal histologically.

Case 8

A housewife aged 56 was first seen in January, 1955, when she gave a 20-years history of progressive polyarthritis which had produced severe crippling. In November, 1954, she had a pyrexial illness with cough and purulent sputum, and since then her hips, particularly the left, had become very painful. On examination she was found to have a severe destructive polyarthritis of all the limb joints, and the left hip was especially painful, being surrounded by tender induration of the soft tissues; there were also nodules on the elbows and elsewhere. E.S.R. 112 mm. (Westergren). *X*-ray examination showed an unusual degree of destruction of the left femoral head with gross excavation of the acetabulum. She was thought to have a secondary infection of the left hip-joint. As she did not wish to enter hospital at that time, she was given a course of penicillin at home by her doctor; a few days later there was a discharge of pus from the left groin and the inflammation surrounding the left hip subsided.

In September, 1955, she was admitted to the infirmary. There was a healed sinus in the left groin, and the problem appeared to be one of severe crippling rheumatoid arthritis. E.S.R. 140 mm. (Westergren), Hb 10 g./100 ml., W.B.C. 4,900, serum albumin 2.6 g./100 ml., globulin 3.2 g./100 ml., S.C.A.T. 64. A flexed and unstable right knee was fixed by compression arthrodesis, and following a course of rehabilitation in the Devonshire Hospital, Buxton, she returned home walking.

In October, 1956, she became ill again with rigors, fever, and pain in the left chest and some swelling in the neck. She was given chlortetracycline. The fever continued, however, and the left hip became swollen and painful, and she was readmitted to the infirmary on November 12. She had remittent fever up to 101° F. (38.3° C.). In addition to the severe active rheumatoid arthritis there was a subcutaneous abscess over the back of the neck and a deep abscess in front of the left hip. Pus aspirated from both sites grew a staphylococcus resistant to penicillin but sensitive to other available antibiotics. Blood culture was sterile. W.B.C. 13,400. She was treated with erythromycin and streptomycin, but the fever continued and the left hip remained painful. On November 19 the left hip was explored and widespread osteomyelitis of the ilium was found. After removal of infected bone the wound was closed. The fever subsided with continuous streptomycin therapy, but after three weeks she developed tinnitus and deafness, and streptomycin was discontinued after she had received a total of 28 g. There has been no recurrence of the bone infection, but she is still crippled by a combination of severe rheumatoid arthritis and vestibular ataxy.

Case 9

A male machinist aged 51 was admitted to the infirmary on December 29, 1952, for severe polyarthritis of two years' duration accompanied by constitutional illness and weight loss of over 30 lb. (13.6 kg.). On admission he was ill with fever up to 100.8° F. (38.2° C.). There was severe inflammatory arthritis of all limb joints and the upper spine, with lymphadenopathy but no other evidence of visceral disease. E.S.R. 61 mm. (Westergren), Hb 11.1 g./100 ml., W.B.C. 7,400, S.C.A.T. 256. He was treated with bed rest, splintage, aspirin, and gold, and on January 19, 1953, he was transferred to the Devonshire Hospital, Buxton, where this treatment was continued, and eventually he made a good recovery, returning home in April and resuming full work a few months later. He had minor joint pains and disability, for which he took 200 mg. of phenylbutazone daily, and in this way continued working until October 8, 1956, when he developed an illness with shivering, malaise, and cough with purulent sputum. After a week in bed he felt better and returned to work, but on October 15 he developed a painful red swelling over the left ankle. Next day the right elbow became painful and got rapidly worse, and in the next few days both knees and the left elbow became swollen and painful.

On October 22 he was readmitted to the infirmary. He was desperately ill, but had only low-grade fever up to 101° F. (38.3° C.). The elbows, knees, and left ankle were hot, swollen, and very painful; the remaining joints showed signs of old inactive rheumatoid arthritis. A few crepitations could be heard in the chest, and he had severe dysphagia due to acute oesophagitis but no other signs of visceral disease. W.B.C. 16,000. Thick yellow pus was aspirated from the right elbow and left ankle; both specimens grew a *Staph. aureus* resistant to penicillin but sensitive to other available antibiotics. A similar staphylococcus was cultured from the blood, and a few days later a similar organism was grown from pus aspirated from both knees and the left elbow.

On the day of admission he was given intra-articular and parenteral penicillin, and then 20 mg. of erythromycin into each infected joint together with intramuscular streptomycin. After a few days the oesophagitis subsided and he could take oral erythromycin, penicillin being discontinued. By November 6 all the infected joints had subsided except for the right elbow, which remained grossly swollen and painful. An abscess over the elbow was evacuated surgically, but

in spite of continued streptomycin and plaster splintage the elbow remained painful and *x*-ray examination showed extensive osteomyelitis of the humerus, radius, and ulna. Amputation was advised but refused, and the osteomyelitis eventually settled with prolonged streptomycin therapy supplemented by courses of other antibiotics. The total dosage was: streptomycin 124 g., erythromycin 21 g., chlortetracycline 5 g., oxytetracycline 10.5 g., chloramphenicol 10.5 g.

In April, 1957, he finally returned home with good function in all the joints except the right elbow, which was ankylosed; since then he has remained in good health except for one mild exacerbation of the osteomyelitis, which resolved with antibiotic therapy.

Case 10

A housewife aged 37 was admitted to the infirmary on January 25, 1957, as an urgency. She had had two attacks of pneumonia as a child and "rheumatism of the arms and legs when aged 15 years, but had otherwise been well until six months previous to admission, when she developed pains over the lower ribs on both sides. These persisted, and three weeks before admission she developed a cough with purulent sputum. On January 18 she became ill with rigors, and the following day she had painful swelling of the finger-joints, the left shoulder, and both forearms. These symptoms were partially relieved by aspirin, but the swellings increased in size.

On admission she was obviously very ill, but had only low-grade fever up to 101° F. (38.3° C.). There were clinical and radiological signs of patchy consolidation of the right lung, slight lymphadenopathy, but no other evidence of visceral disease. Multiple subcutaneous and intramuscular abscesses were present over the upper limbs and chest wall, but no definite signs of arthritis. She also had a foul vaginal discharge. E.S.R. 115 mm. (Westergren), Hb 10 g./100 ml., W.B.C. 10,200, S.C.A.T. 8, serum albumin 2.9 g./100 ml., globulin 3.9 g./100 ml. Pus aspirated from several abscesses grew a *Staph. aureus* sensitive to penicillin and other available antibiotics. A similar organism was grown from the sputum and a high vaginal swab. One blood culture was sterile. She was treated with penicillin, 1 mega unit six-hourly, and streptomycin, 2 g. daily, and made a rapid and uneventful recovery, but three months later she still complained of some pain and stiffness in the joints. In this case the evidence of rheumatoid arthritis is very doubtful and the sheep-cell agglutination titre was only 8.

Case 11

A male cotton-worker aged 39 was first admitted to the infirmary on December 10, 1956, because of severe polyarthritis of six months' duration associated with malaise and weight loss of over 28 lb. (12.7 kg.).

On admission he was ill with irregular fever up to 100° F. (37.8° C.). He had a severe symmetrical polyarthritis of all the limb joints and the cervical spine. He had nodules on the elbows, lymphadenopathy, and slight splenic enlargement but no other signs of visceral disease. E.S.R. 94 mm. (Westergren), Hb 12.1 g./100 ml., W.B.C. 6,000, S.C.A.T. 256. Two tests for L.E. cells were negative. He was treated with prednisolone. Though even a dosage of 30 mg. daily produced only partial suppression of his arthritis, he improved sufficiently to leave hospital and return to work.

In June, 1957, he developed slight dyspepsia and a few days later profuse uncontrollable gastric bleeding, for which an emergency gastrectomy was performed in a local hospital. Following this, steroid therapy was withdrawn and on July 12 he was readmitted to the infirmary because of a severe flare-up of his polyarthritis. He was desperately ill, with a fever up to 102° F. (38.9° C.). All the limb joints were swollen and painful and the laparotomy wound was incompletely healed. E.S.R. 120 mm. (Westergren), Hb 8.3 g./100 ml., W.B.C. 6,500, S.C.A.T. 1024, serum albumin 1.8 g./100 ml., globulin 4.3 g./100 ml. During the following days he had several mild rigors, and the right knee, left tarsus, and right olecranon bursa became more painful, and a swelling appeared below the right scapula. There was also some fluctuation in the right calf beneath a slightly inflamed saphenous vein.

On July 25 culture was made of blood and of pus aspirated from the swelling in the calf; and both specimens grew a *Staph. aureus* resistant to penicillin, streptomycin, and tetracycline but sensitive to chloramphenicol, erythromycin, and novobiocin. He was treated with local and oral erythromycin, and two days later pus was aspirated from the knee, but this was sterile; a few days later pus was aspirated from the scapular swelling, and this grew a staphylococcus similar to the one obtained from the blood. The abscesses and the acutely inflamed joints were treated by repeated aspiration and intra-articular erythromycin. He was given a course of oral erythromycin totalling 12 g. followed by novobiocin (10 g.). By mid-August his fever had subsided and all abscesses had resolved. A troublesome candida infection of the mouth was controlled with nystatin. His rheumatoid arthritis, however, remained active and fever reappeared, rising to 104° F. (40° C.), but there were no rigors and no other evidence of bacterial infection.

On August 16 corticotrophin therapy was started with satisfactory control of fever. The initial dose was 10 units of corticotrophin gel twice daily; the urinary 17-ketogenic steroids at that time were 11.7 mg./24 hours. After one month the ketogenic steroids had fallen to 3.5 mg. per 24 hours and the dose of corticotrophin was gradually increased until the end of December, when he was receiving 20 units twice daily and the ketogenic steroids had risen to 10 mg. per 24 hours. By this time he was well enough to return home for Christmas, but the S.C.A.T. had risen to 2048. While at home he had two episodes of gradual loss of consciousness, and on January 2, 1958, he was readmitted to the infirmary, where he was found to have severe uncontrollable melaena. The abdomen was reopened and a bleeding stomal erosion undersewn. This operation was covered by continuous blood transfusion and corticotrophin therapy, with a course of oxytetracycline.

During the first week progress was satisfactory, but on January 10 he developed remittent fever up to 101° F. (38.3° C.) and a sudden increase of pain and swelling in the following joints: left wrist, elbow, and third proximal interphalangeal joint, and right knee and fifth metatarsophalangeal. Pus was aspirated from these joints, and a *Staph. aureus* resistant to penicillin, streptomycin, and tetracycline was cultured from all specimens. He was treated with intra-articular and oral erythromycin. At the time of writing he was still gravely ill, but this second episode of staphylococcal infection appears to have been controlled, and he had retained good function in all the infected joints.

Case 12

A retired officer aged 60 was admitted to the infirmary on June 19, 1957. For 20 years he had suffered from a steadily progressive rheumatoid arthritis that had produced severe crippling. In January, 1957, he developed pleuritic pain in the left lower chest; two weeks later a swelling appeared below the left scapula, and in a few days this discharged blood-stained pus. In February a similar sequence of events occurred on the right side of the chest and he was left with two discharging sinuses. His general condition deteriorated slowly, but it was not until June that he became seriously ill and his right knee became increasingly painful and swollen.

On admission he was extremely ill, but had only low-grade fever up to 101° F. (38.3° C.). He had severe destructive polyarthritis affecting all the limb joints and the upper spine; but the right knee was especially painful, swollen, and hot. There were multiple subcutaneous nodules, some of which were ulcerating, and discharging sinuses were present over the lower ribs on both sides of

the back. Clinical and radiological signs suggested small bilateral empyemata. There was generalized lymphadenopathy, but no other evidence of visceral disease. E.S.R. 100 mm. (Westergren), Hb 8.5 g./100 ml., W.B.C. 22,000, S.C.A.T. 256, serum albumin 2.4 g./100 ml., globulin 3 g./100 ml. Pus aspirated from the right knee and both pleurae, a swab taken from an ulcerating subcutaneous nodule, and a blood culture all grew a *Staph. aureus* resistant to penicillin but sensitive to other available antibiotics.

He was given 0.5 g. of oxytetracycline intravenously, and later 1 g. six-hourly by mouth, but he continued to be desperately ill with intermittent pyrexia up to 102° F. (38.9° C.) and developed a candida throat infection which was controlled with nystatin. On July 27 the pyarthrosis of the right knee was still progressing and *x*-ray examination showed extensive osteomyelitis of the femur and tibia. An emergency mid-thigh amputation was performed by Mr. Lloyd Griffiths, under cover of intravenous oxytetracycline and 1 g. of streptomycin intramuscularly. On July 28 the antibiotic was changed to erythromycin, 1 g. six-hourly. Following this the fever settled, and two weeks later fluid from the left knee and pleurae was sterile and a swab from the chest sinus grew only coliforms. The amputation wound healed, as did both chest sinuses, and he returned home learning to walk on crutches.

Diagnosis

Most of the patients in this series were suffering from severe active rheumatoid arthritis, so that some increase of pain and swelling in several joints accompanied by deterioration in general health was naturally attributed at first to an exacerbation of the rheumatoid process, and in the early cases the correct diagnosis was made only when a swelling unexpectedly discharged pus, as in Cases 1 and 2, or when multiple osteomyelitis or pyarthrosis was found at necropsy, as in Cases 4, 5, and 6. One of the major difficulties was the absence of the normal response to bacterial infection with pyogenic organisms in some cases. For instance, Case 3 remained afebrile throughout and had white cell counts of 4,300 and 5,800, although staphylococcal pus was present in three large joints. In Case 5 significant fever appeared only a few days before death, and the highest white-cell count recorded was 5,200, although the patient died of a pyarthrosis of the right shoulder. Other cases already had fever from the active rheumatoid disease, and it was only when the fever increased and became remittent that it gradually became apparent that some infective process had supervened.

In retrospect the most useful indication of bacterial infection was the occurrence of rigors. In response to questioning a history of rigors at the presumed onset of infection was obtained in all patients except Case 4. The rigors were usually followed by a rapid deterioration in general health and a rather sudden increase of pain and swelling in one or more joints.

In Cases 7, 9, and 10 the bacterial infection began in the classical manner with rigors and fever, and it was only the previous history of arthritis and the occurrence of pain and swelling in many joints that caused confusion. Once the possibility of an acute bacterial polyarthritis was considered these cases presented no difficulty.

By far the most useful investigation was aspiration of the more painful joints, and in the light of our experience with these patients aspiration and culture of fluid from the more painful joints are indicated in every patient with rheumatoid arthritis in whom there is a sudden deterioration, especially if there has been a rigor. In such cases repeated blood culture is also required, but unless all suspected joints are aspirated a large collection of pus may remain unrecognized and undrained, with fatal outcome.

The greatest difficulty was encountered in Case 4 because the purulent sputum and the radiological and clinical signs all suggested bronchopneumonia, and yet no pathogenic organism could be grown from the sputum, blood culture remained sterile, and the infecting staphylococcus was grown only from the sacral abscess that appeared a few days before death. The widespread suppuration in the ribs was never suspected during life.

Localized suppuration in ribs or chest wall occurred in 5 out of the 12 patients. This unusual localization of suppuration would seem to be characteristic of rheumatoid arthritis, so that such a lesion should be deliberately looked for in any patient with rheumatoid arthritis in whom bacterial infection is suspected.

Radiological investigation was relatively unhelpful. Extensive radiological surveys of the joints of many of the patients revealed severe osteoporosis and extensive articular erosion characteristic of rheumatoid arthritis, and these changes made it difficult to recognize the superimposed lesions of bacterial infection. Chest films were often misleading, suggesting possible bronchopneumonia as the cause of the illness when the problem was really one of suppuration in the bones and joints. Only in Cases 8, 9, and 12 were the radiographs really helpful in demonstrating the extent and severity of the osteomyelitis.

The true nature of the illness may also escape notice at necropsy unless a systematic examination of the bones and joints is carried out: With the exception of Case 7, in which a bacterial endocarditis of the tricuspid valve had led to septic infarcts of the lungs, visceral abscesses were not encountered; and in most cases it seems unlikely that a firm diagnosis of widespread suppuration could have been made from histological study of the internal organs, particularly when the condition had remained unrecognized before death.

In summary, it would appear that widespread infection of joints and bones should be suspected in any patient with rheumatoid arthritis in whom there is a sudden deterioration or an unexplained remittent fever, especially if a history of rigors can be elicited. Aspiration of all the more painful joints with culture of the joint fluid, and repeated blood cultures, are required, since this appears to be the only certain way of arriving at a correct diagnosis.

Treatment

Although five out of our first seven patients died, it would appear that the prognosis can be much improved, provided that the correct diagnosis of suppurative bacterial infection is made at an early stage and the infecting organism can be cultured from either the blood or infected joint, so that its sensitivity to the available antibiotics can be assessed. Once this information is obtained, appropriate antibiotic therapy must be continued until the patient recovers. Since bacterial infection of bone is difficult to eradicate, antibiotic therapy may have to be continued for many weeks. The other essential measure is a daily search for collections of pus either in joints or bursae or in the soft tissues or pleurae, because in these patients with severe rheumatoid arthritis soft-tissue abscesses or pyarthroses may develop with minimal local signs of inflammation and large collections of pus may easily be missed.

Collections of pus may at first be treated by aspiration and local instillation of an appropriate antibiotic, but if they cannot be rapidly sterilized in this way surgical drainage should be carried out. With early diagnosis and energetic treatment some of these rather desperate cases seem to make an excellent recovery and their rheumatoid disease appears to remit for some years, so that they return to a useful and happy life. These suppurative complications should therefore not be thought of as a terminal event in an incurable disease.

Discussion

Suppurative arthritis is now rarely seen in hospital practice. A review of the 91,815 admissions to the Manchester Royal Infirmary during the period 1950–7 inclusive produced only 13 additional cases of suppurative arthritis. In a woman aged 20 there was a subacute polyarthritis

TABLE III.—*Details of Patients with Suppurative Arthritis Only*

Case No.	Age	Sex	Other Diseases	Trauma	Infection		
					Site	Organism	Outcome
1	33	M	Diabetes and boils	Blow on R. ankle	R. ankle	*Staph. albus*	Recovered
2	13	M	None	Needle in R. wrist	R. wrist	—	,,
3	67	F	,,	None	R. ankle	Pneumococcus	,,
4	7	M	,,	Fall on L. shoulder	L. shoulder and humerus	*Staph. aureus*	,,
5	9	M	Boils	None	L. knee and femur	,, ,,	,,
6	23	M	R. tennis elbow	Injection of R. elbow	R. elbow	,, ,,	,,
7	39	M	None	Tooth wound, L. hand	L. 3rd metacarpo-phalangeal joint	*Staph. albus.*; anaerobic strep.	,,
8	29	M	,,	None	L. knee	Gram-positive cocci in smear. Culture (after 4 days' penicillin) sterile	,,
9	42	M	Epididymo-orchitis	,,	L. knee	*Staph. aureus*	,,
10	24	F	Puerperal sepsis	,,	L. shoulder	*Staph. albus*	,,

associated with vaginal discharge, but no pathogenic organism was isolated from either joints or genital tract and there was no obvious response to two courses of penicillin, so that the diagnosis in this case seems doubtful. In the remaining 12 the arthritis was strictly monarticular. In a woman aged 66 who died of suppurative cholangitis and megaloblastic anaemia a pyarthrosis of one knee was found at necropsy. In a youth aged 17 severe meningococcal septicaemia was complicated by a transient arthritis of one elbow. The remaining 10 cases, which are summarized in Table III, conform to the classical description of monarticular suppurative arthritis associated in most cases with trauma, penetrating wounds, or an obvious source of infection. The diagnosis presented no difficulty, the response to antibiotic therapy was prompt, and with the exception of the two children with osteomyelitis the illness was never serious.

This picture differs strikingly from the serious polyarticular suppurative disease seen in our patients with rheumatoid arthritis. Furthermore, it appears that our cases account for half of the total cases of suppurative arthritis admitted to this large general hospital, which makes it very unlikely that our cases represent a chance association between suppurative arthritis and rheumatoid arthritis. In a follow-up study of patients with rheumatoid arthritis admitted to the Massachusetts General Hospital, Cobb *et al.* (1953) found an excess mortality from bacterial infection, and in a field survey Miall (1955) found an increased incidence of tuberculosis in individuals with rheumatoid arthritis. There is therefore some evidence to suggest that individuals with rheumatoid arthritis are abnormally susceptible to bacterial infection, and this seems the most likely explanation in our cases.

The administration of corticotrophin or adrenocortical steroids in high dosage predisposes to bacterial infection, and Mills *et al.* (1957) have reported two cases of suppurative arthritis complicating such treatment, given in one instance for systemic lupus erythematosus and in the other for exfoliative dermatitis. Of our 12 cases, only four had had any such hormone therapy, and in only two was this being given at the time of the presumed onset of the infection. Agranulocytosis was not present in any of our cases. Although white-cell counts of 3,000–5,000 were commonly observed before the onset of infection, the differential counts were all normal. Some degree of acquired agammaglobulinaemia seems a remote possibility, since the serum globulins were generally not as high as might have been expected, but in the four cases in which electrophoretic data are available gamma-globulin was present in normal or slightly increased amounts. On the other hand, total serum proteins were on the low side, the mean for the group being 5.92 g./100 ml., with albumin 2.75 and globulin 3.17 g./100 ml.

A study of the sheep-cell agglutination titres did not reveal any constant peculiarity, though in some cases the titres were unexpectedly low during the episode of bacterial infection.

It was not possible to determine with certainty the source of the infecting organisms in our 12 cases. The condition was recognized only in the late stages of the disease—sometimes, in fact, only at necropsy. A positive blood culture was obtained on six occasions, but in each instance this was the result of an overflow from the infected joints and indicated some form of severe infection.

It is accepted that a transient bacteriaemia is possible in mild infections and that it may also be found in the absence of any obvious infection. In 2 of our 12 cases a coliform urinary infection was present and the same organism was responsible for the arthritis; in six cases there was a purulent infection of the respiratory tract, and in most of these *Staph. aureus* was the responsible organism; in three cases the polyarthritis was preceded by ulceration and infection of subcutaneous nodules, from which *Staph. aureus* was isolated; in Case 11 *Staph. aureus* was isolated from three joints and also from nasal swabs; the phage type of these strains was the same, indicating that the organisms, normally present in the nose, were ultimately responsible for the infected joints.

Staph. aureus and *Escherichia coli* are widely distributed and tend to be present in large numbers on the mucous membranes and skin. They are responsible for a wide range of infections, and a transient bacteriaemia is probably not an uncommon phenomenon. Normally the defence mechanism readily eliminates these organisms, but when there is damaged or abnormal tissue with reduced resistance the organisms are more apt to localize and produce infection.

Summary

Twelve cases are reported in which rheumatoid arthritis was complicated by severe bacterial infection of connective-tissue structures. In nine this was mainly a suppurative arthritis which was often polyarticular, resembling an exacerbation of the rheumatoid process.

The infecting organisms were coliforms in two cases and staphylococci in ten, of which only three were sensitive to penicillin. The febrile and leucocytic response to infection with these organisms was often modified or absent, and in some instances the widespread suppuration was revealed only by a systematic examination of the joints at necropsy.

The diagnostic problems posed by these cases are discussed and it is concluded that this condition is probably not rare but may often remain unsuspected even after death. If the infecting organism can be cultured from joints or blood at an early stage, appropriate antibiotic therapy can give excellent results in what must otherwise be a fatal condition.

POSTSCRIPT.—Since the preparation of this paper an additional case has come to our notice in a man aged 70 who had severe nodular rheumatoid arthritis of 35 years' duration. During the autumn of 1957 his condition deteriorated, and on November 16 he fell, fracturing the right femoral neck. This was treated with a compression screw, but his general condition worsened steadily and he died on January 27, 1958, for no apparent reason. Necropsy revealed unsuspected pyarthrosis of most of the major limb joints, and

pus from three of these joints produced a pure culture of *Staph. aureus* resistant to penicillin, streptomycin, and tetracycline.

We are grateful to Dr. H. S. Barber for allowing us to publish details of the two patients who were under his care. We thank the members of the medical and nursing staff of the Manchester Royal Infirmary who have helped in the diagnosis and care of these difficult cases, and the members of the laboratory staff for much technical assistance.

REFERENCES

Bywaters, E. G. L. (1953). *Ann. rheum. Dis.*, **12**, 114.
Cobb, S., Anderson, F., and Bauer, W. (1953). *New Engl. J. Med.*, **249**, 553.
Coste, F., Delbarre, F., and Basset, G. and F. (1957). In F. Coste's *Le Rhumatisme*, 5th series, p. 113. Expansion Scientifique Française, Paris.
Miall, W. E. (1955). *Ann. rheum. Dis.*, **14**, 150.
Mills, L. C., Boylston, B. F., Greene, J. A., and Moyer, J. H. (1957). *J. Amer. med. Ass.*, **164**, 1310.

BACTERIAL FLORA OF THE UPPER RESPIRATORY TRACT IN PADDINGTON FAMILIES, 1952–4

BY

P. L. MASTERS, M.D., D.C.H.

W. BRUMFITT, M.D., M.R.C.P.

R. L. MENDEZ,* M.B., B.S.

AND

M. LIKAR, M.D.

From Paddington Green Children's Hospital and the Wright–Fleming Institute of Microbiology, St. Mary's Hospital Medical School, London

This paper presents the bacteriological findings of a survey of respiratory disease among families in the Paddington area. The regular visits to the families provided a unique opportunity to sample the upper respiratory flora of the family members and to correlate the information obtained with the clinical and epidemiological findings. Previous workers have studied adults and children separately (Straker, Hill, and Lovell, 1939) or a particular organism (Cunliffe, 1949; Holmes and Williams, 1954; Breese and Disney, 1956), but this seems to be the first long-term investigation of the upper respiratory flora of families.

The families were recruited from those who brought a child to Paddington Green Children's Hospital for medical advice. They were included in the survey only if they consisted of father, mother, and three children (at least one of which was under 5 years of age) and lived as a separate and independent household. By confining the survey to families of the same size and similar structure it was hoped to be able to assess more accurately the effect of different domestic conditions, such as housing, nutrition, cleanliness, and maternal care, on the introduction and spread of respiratory disease.

Brimblecombe *et al.* (1958) have described the methods and epidemiological results of the survey, in which were recorded the incidence and spread of respiratory pathogens in families in relation to environmental factors such as crowding and climate. The purpose of this paper is to give the bacteriological findings in greater detail. These are based on the results of over 9,000 nose and throat swabs taken fortnightly from 72 families, most of whom were swabbed for more than a year, and of 700 pairs taken daily or three times a week from 10 families, each swabbed for four weeks.

We aimed to develop and test simple techniques for isolating and identifying respiratory pathogens and for increasing their yield by enrichment. We also wished to determine the isolation rates of each main pathogen in the nose and throat for different age groups and different seasons, and to gain information on the carriage and spread of specific bacterial types in the survey families.

Techniques

Standard Methods

Pernasal and throat swabs with dry cotton-wool tips were taken from each available member of a family every fortnight. The pernasal swabs were made with thin flexible wire so that they could be introduced well into the nose without discomfort. The throat swabs were rubbed over both tonsils and the posterior pharyngeal wall.

Within two hours of being taken the swabs were streaked on to 5% blood agar (B.A.) and the same medium with the addition of 1 : 500,000 crystal violet (B.V.). The swab was used to inoculate a small portion of the plate, and this inoculum was spread with a wire loop in the standard fashion over half the B.A. plate and over a quarter of the B.V. plate. The "plating" was carried out by the same two operators throughout the survey. The plates were incubated aerobically at 37° C. and inspected after 18 hours. It was found that the size of the bacterial colonies and the mucoid character of colonies of pneumococci were enhanced by placing large trays of water at the bottom of the incubator to keep the atmosphere moist.

The bacterial species identifiable on these two culture media included staphylococci, haemolytic streptococci, pneumococci, *Haemophilus influenzae*, and coliform organisms. Meningococci were searched for during the first two months of the survey without success, perhaps because the plates were incubated for only 18 hours.

In addition to the two media described, Hoyle's tellurite agar was inoculated in the first two months of the survey, but was abandoned because no diphtheria bacilli were isolated. During most of the second year of the survey quarter-plates of nutrient agar containing 5% Fildes peptic digest of blood and 1 : 500,000 crystal violet (F.V.) were inoculated in addition to the other two media to improve the isolation of haemophili.

The plates were inspected in a good light with the aid of a watchmaker's lens, which was found more convenient for identifying and subculturing colonies of pneumococci, etc., than the dissecting microscope favoured by the Commission on Acute Respiratory Diseases (1948).

The number of each suspected bacterial pathogen present on the plate was estimated roughly as follows: confluent growth was recorded as +++, over 20 colonies but not confluent as ++, and fewer than 20 colonies as +. Further identification of each species was made by the methods described below.

Pneumococci

Samples of each kind of smooth or flat colony showing green zones on either the B.A. or B.V. plate were streaked in parallel rows on a B.A. plate. Before incubation a strip of blotting paper 1 by 8 cm. on which had been dried eight 20-c.mm. drops of 1:2.000 "optochin" was laid on the plate at right angles to the inoculated streaks. After

*Dr. Mendez died on April 27, 1953.

overnight incubation subcultures showing a zone of inhibition extending more than 5 mm. from the edge of the strip were typed by the capsular swelling technique, using the full range of 46 sera supplied by the State Serum Institute, Copenhagen. Cultures showing no zone of inhibition were classified as *Streptococcus viridans*. Cultures showing zones of inhibition intermediate in width were uncommon, and whenever tested for bile solubility proved to be *Str. viridans*.

Staphylococci

Staphylococci were classified mainly by means of the slide coagulase test. Strains with typical morphology on Gram-staining were classified as *Staphylococcus pyogenes* if the coagulase test was positive and *Staph. albus* if it was negative. Only *Staph. pyogenes* was recorded as a positive finding in the analyses.

Haemolytic Streptococci

Representative colonies from both blood plates showing zones of complete or partial haemolysis were subcultured on to B.A. plates. If the subculture was pure, haemolysis complete, and morphology typical in a Gram-stained film, those cultures were classified as beta-haemolytic streptococci. This last step was important in excluding haemolytic haemophili, which were often present. During the first year of the survey most of the beta-haemolytic streptococci were tested for Lancefield group A by the precipitin test, using the enzyme produced by *Streptomyces albus* to prepare the extracts (Maxted, 1948). Six months after the survey began the bacitracin method of identifying group A streptococci (Maxted, 1954) was adopted by placing bacitracin squares on the subculture plates. The use of the two methods together during the second six months provided a valuable check on technical methods. From the end of the first year the bacitracin-sensitive strains were sent to the Streptococcal Reference Laboratory at Colindale, where Dr. R. E. O. Williams kindly arranged for them to be typed.

Haemophili

In cultures from the fortnightly swabbings attention was confined to the capsulated strains of *H. influenzae* because these are typable and therefore of epidemiological interest. During the period of frequent swabbing non-capsulated haemophili were also recorded.

During the first year of the survey small mucoid translucent colonies on B.A. or B.V., often suspected of being haemophili by showing satellitism with colonies of staphylococci and other bacteria, were subcultured on to boiled blood agar. If the growth showed the typical morphology of *H. influenzae* on a Gram-stained film it was tested for slide agglutination with the antisera to Pittman types *a* to *f*. About half the cultures suspected of being capsulated from their colonial appearance were not typable: many of these agglutinated slowly in one or more of the six antisera or occasionally in saline.

In the second year F.V. was used as a primary plate to help isolate and identify the Pittman strains. It was found that preparation of the peptic blood broth by incubation in the 50° C. water-bath for as long as 48 hours gave the best results both in increasing the size of the colonies of haemophili and in reducing the growth of streptococci and pneumococci. So prepared, F.V. is a relatively selective medium for haemophili, but it allows the growth of coliform bacilli, which produce large semi-translucent iridescent colonies, and of crystal-violet-resistant neisseriae and micrococci, which usually produce opaque colonies. The capsulated haemophili form translucent, strongly iridescent, and coalescent colonies. The non-capsulated strains form translucent colonies which usually lack both iridescence and coalescence.

The growth requirements of the haemophili were not determined routinely, but 27 colonially typical strains isolated on F.V., two of them capsulated, were investigated by the plate method of Everall (1953) in which two blotting-paper strips, one containing X factor and the other V factor, are laid on nutrient agar at right angles to the inoculum: 24, including the two capsulated strains, required both X and V factors (*H. influenzae*), and three required X factor only. Four haemolytic haemophili isolated from blood agar required V factor only.

Coliform Bacilli

Under this heading were included Gram-negative bacilli producing large greyish-white colonies, and also proteus-like strains. No attempt was made to investigate them further in the routine survey.

Enrichment and Frequent Swabbing

In December, 1953, one family was swabbed daily, except on Sundays, for four weeks. In each of the months January, February, and March, 1954, three families were swabbed three times a week for four weeks. Three of these nine families were chosen from each of the overcrowded, crowded, and uncrowded categories (Brimblecombe *et al.*, 1958). Finally, in June, 1954, one of the families swabbed in March was swabbed thrice weekly for another four weeks.

During the period of frequent swabbing an enrichment technique was used in addition to the standard methods just described. After being used for plating, each swab was thrust into a solid enrichment medium (CVN_3) described by Holmes and Lermit (1955) and adapted from an enrichment broth described by Pike (1944). The medium consisted of 5% horse blood in nutrient agar (blood agar base, "oxoid") containing 1:500,000 crystal violet and 1:16,000 sodium azide. It was distributed in 5-ml. amounts in test-tubes 6 by $\frac{5}{8}$ in. (15 by 1.6 cm.) with aluminium caps. When a swab was thrust into the medium its cotton-wool plug replaced the aluminium cap. After incubation at 37° C. for 18 hours each swab was taken out and used to inoculate F.V. plates for haemophili and a medium consisting of 5% horse blood in nutrient agar containing 1:500,000 crystal violet and 2 μg. of streptomycin per ml. (B.V.S.), which is a selective medium for pneumococci and streptococci.

Before inoculation of the B.V.S. plates an optochin strip was placed on the medium across the middle of each plate. A quarter of a plate was used for each swab, which was streaked out at right angles to the optochin strip. In this way most growths of pneumococci were identified without subculture.

Results

The results of the fortnightly swabbings have been analysed in the report by Brimblecombe *et al.* (1958) mainly for comparison with the clinical data in relation to factors which may affect the incidence and spread of acute respiratory infections. They were also used to follow seasonal fluctuations in the isolation rates of pneumococci, *Staph. pyogenes*, and haemolytic streptococci over a period of two years. There was a tendency for pneumococci to be isolated more often in the winter months and for *Staph. pyogenes* to be isolated more often in the summer months, while haemolytic streptococci showed no consistent seasonal trend in isolation rate. The findings reported here concern mainly the incidence of different respiratory pathogens related to age and site in the upper respiratory tract.

The results of the frequent swabbings have also been analysed to show the effect of nasal discharge on the isolation rates of some respiratory pathogens and the effect of the enrichment method on isolation rates in relation to age and nasal discharge. On the epidemiological side the combination of the enrichment technique with frequent swabbing enabled the spread of specific bacterial types within the families to be followed with greater accuracy than was possible with the fortnightly swabbings.

The findings from 520 pernasal and throat swabs (swab-pairs) taken from the nine families swabbed frequently during January–March, 1954, were used to assess the effect of the enrichment technique on the isolation rates of five respiratory pathogens. The percentage of positive swab-pairs by direct plating and the percentage positive after

adding the results of enrichment were as follows: pneumococci, 51 and 70; non-capsulated haemophili, 50 and 70; group A streptococci, 13 and 23; coliform bacilli, 10 and 22; and capsulated haemophili, 3 and 5. There were considerable differences between families in the extra yield of organisms from enrichment.

Pneumococci

Fig. 1 compares the isolation rates of pneumococci from the nose and throat swabs taken fortnightly with those taken from the nine families frequently swabbed during January–March, 1954. From the nose swabs high isolation

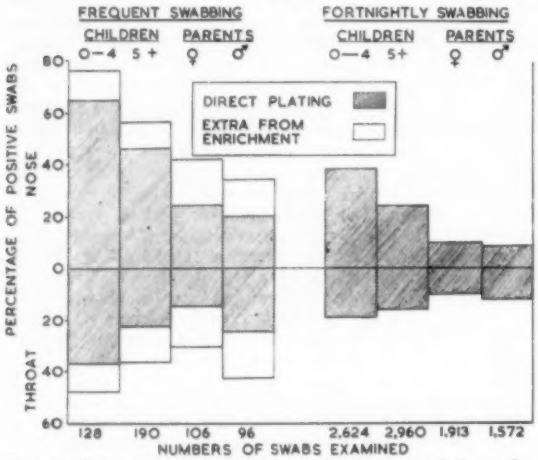


FIG. 1.—Pneumococcal isolation rates from nose and throat by age groups.

rates of pneumococci in the young children and a steady decline with age were found in both groups. Differences in the isolation rates from throat swabs at different ages were slight. The proportion of extra isolations obtained by enrichment increased with age, but not enough to eliminate the downward trend in nasal isolation rates with age. The higher rates for the frequently swabbed families compared with the fortnightly swabbings are attributable largely to the higher pneumococcal incidence associated with nasal discharge found in the winter months, but family differences play a part. The considerable differences between families in pneumococcal incidence are illustrated by Table I, in which the effect of seasonal variations was avoided by including only the swabbing results of the first 12 months for the 45 families which were swabbed for at least a year.

TABLE I.—*Differences of Pneumococcal Incidence in the 45 Families Swabbed for at Least a Year*

	Percentage Range of Positive Swab-pairs					
	1–10	11–20	21–30	31–40	41–50	Over 50
No. of families ..	0	8	19	12	6	0

Fig. 2 compares the effect of nasal discharge in the children and parents on the pneumococcal isolation rates from nose and throat swabs. If the results of direct plating are considered, nasal discharge in the children is associated with a higher isolation rate from both nose and throat swabs, while nasal discharge in the parents is associated with a higher isolation rate from nose swabs only. If the results of enrichment are included, only the children show a higher isolation rate in the presence of nasal discharge. This difference from the results of direct plating is due to the enhancing effect of enrichment being greater in the parents than in the children and in the absence of nasal discharge than in its presence.

Fig. 3 shows for the survey as a whole the age distribution of the subjects with the seven commonest pneumococcal types as a percentage of the pneumococci isolated from each of these age groups. The four commonest types —6, 23, 19, and 14 —show a disproportionately high incidence in the pre-school (0–4 years) group.

The results of the frequent swabbing show that many of the individuals were persistent carriers. Sixteen of the 27 children and 6 of the 18 parents carried pneumococci continuously during the four weeks for which they were swabbed. In five of the children and two of the parents there was a change in the type of pneumococcus carried: in one instance a new type was added to the old. The types of pneumococcus carried persistently usually appeared sporadically in the nose or throat of other members of the family. One family swabbed during March was swabbed for a second four-weeks period during June. The three children were carrying the same types of pneumococci throughout both periods.

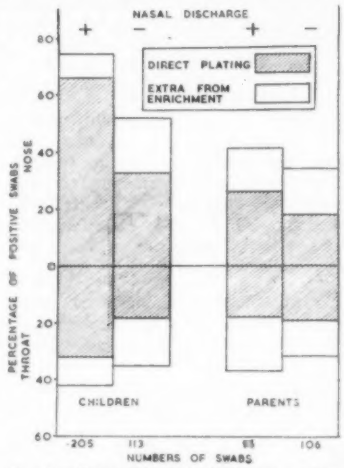


FIG. 2.—Effect of nasal discharge on the isolation of pneumococci in the frequently swabbed families.

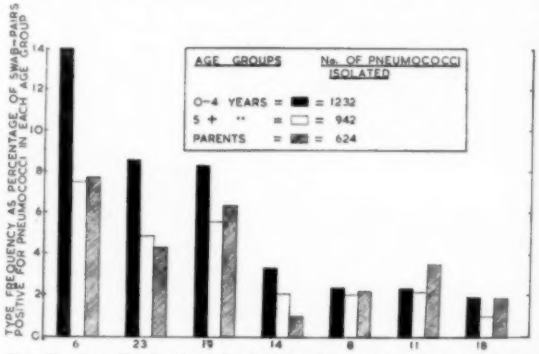


FIG. 3.—Age distribution of subjects with the commoner pneumococcal types.

With the fortnightly swabbings a particular pneumococcal type was often isolated from consecutive swabs of an individual for several months. Prolonged carriage was most frequent with types 6, 19, 23, and 34.

Table II analyses the results of the appearance of new pneumococcal types in the frequently swabbed families. Thirteen new types were introduced into the nine families.

TABLE II.—*Introduction, Persistence, and Spread of New Pneumococcal Types in Frequently Swabbed Families*

Age Groups:	0–4	5+	Mother	Father	Total
No. in each age group ..	11	16	9	9	45
Introducers	1	5	2	5	13
Persistence in Introducers	1	5	2	0	8
Spread from	0	3	2	0	5

Eight of them persisted at least until the next swabbing two or three days later, and five of these eight spread to a total of eight other members (within three days in four instances

and after four to sixteen days in the remaining four). The transferred pneumococci persisted in four of the recipients. Table II shows that the schoolchildren and fathers were the main introducers, although persistence in the fathers and spread from them did not occur. If the introducers and recipients are considered together, persistence of the new types occurred 9 out of 10 times in the children and only 3 out of 11 times in the adults.

Haemophili

Non-capsulated haemophili were not recorded for the fortnightly swabbings, but their incidence in the frequently swabbed families is shown in Fig. 4. The nasal carrier rates according to age resemble those of the pneumococci, but there is a higher throat incidence at all ages.

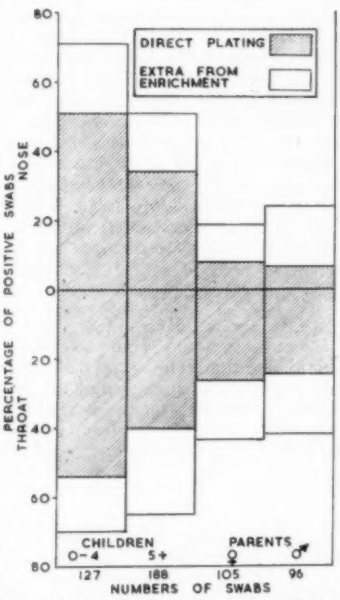


FIG. 4.—Incidence of non-capsulated haemophili in the frequently swabbed families.

A comparison of the incidence of non-capsulated haemophili in the presence and in the absence of nasal discharge in both children and adults gave results similar to those for pneumococci: nasal discharge is associated with a higher nasal carriage on direct plating in both children and adults, but use of the enrichment method eliminates this difference in the adults.

Complete figures for the incidence of capsulated haemophili in the survey cannot be given owing to the lack of Pittman type *a* antiserum for the first five months and changes in the technique of isolation. Fig. 5 gives the incidence for the 12 four-weeks periods during which F.V. was used. The distribution by age and between nose and throat is similar to that of the non-capsulated haemophili, although the incidence is only about a tenth as great. The distribution of the six Pittman types shown in Table III is not a representative sample, since about half of the type *b* strains were isolated during the last three months of the survey. However, the age incidence of Pittman *b* strains (Fig. 5) shows that four-fifths of them were isolated from the pre-school children (0–4 years). Fothergill and Wright (1933) found that over four-fifths of cases of meningitis due to *H. influenzae* type *b* occurred in children up to 3 years old.

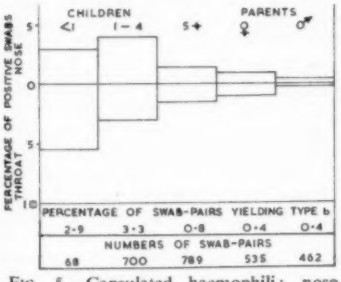


FIG. 5.—Capsulated haemophili: nose and throat incidence.

Two children in the frequently swabbed families carried capsulated strains (types *b* and *e*) of *H. influenzae* throughout the four-weeks period of swabbing. One child belonged to the family which was swabbed again three months later; she was found still to be carrying a type *b* strain during the second four-weeks period.

TABLE III.—*Capsulated Haemophili: Incidence of Pittman Types*

Type No.	*a*	*b*	*c*	*d*	*e*	*f*
	17	35	5	1	13	9

Haemolytic Streptococci

Fig. 6 shows the incidence of haemolytic streptococci in the nose and throat swabs taken fortnightly. Owing to incomplete Lancefield grouping in the first nine months of the survey the results for this period have been omitted in the figure. They do not differ materially in other respects from those in the remainder of the survey.

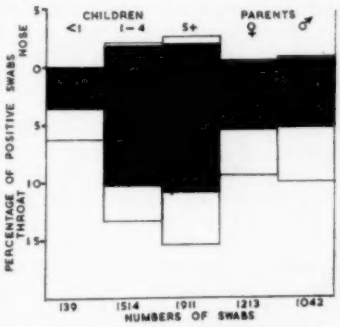


FIG. 6.—Haemolytic streptococci: nose and throat incidence by age groups. Black areas=Group A streptococci. White areas=Other haemolytic streptococci.

The incidence of haemolytic streptococci was about twice as great in the schoolchildren and pre-school children of 1 to 4 years as in the parents, and the excess was almost entirely due to group A streptococci. This group also accounted for nearly all the haemolytic streptococci isolated from nose swabs. Both in children and in adults isolations from throat swabs were much commoner than from nose swabs.

Typing of the group A streptococci enabled data to be collected on the carriage and spread of specific types. Among the 45 members of the frequently swabbed families there were 9 continuous carriers, 8 of them children. One child showed a change of type carried. Sporadic appearance of the carried type in the nose or throat of other members of the family was common. Three new types of group A streptococci appeared in the nine families. One replaced another type in the throat of a boy aged 3 years who developed sore throat and fever two days after the new type appeared, followed by nasal discharge three days later and earache with discharge nine days later. Another appeared in the throat of a girl aged 8 years who developed cough and nasal discharge one day later. The third new type appeared in the nose of another girl of 8 years who developed nasal discharge two days later. Although the appearance of all three types was followed by upper respiratory symptoms, this does not imply that all the symptoms were necessarily due to streptococci. None of the three types spread to other members of the family during the remainder of the four-week periods (one, one, and three weeks).

Table IV analyses for the fortnightly swabbings the introduction and spread of 74 new types of group A streptococci into the families. On the average a child introduced and received more than twice as many new types as did a parent.

TABLE IV.—*Introduction and Spread of Types of Group A Streptococci in Families Swabbed Fortnightly*

Category of Streptococcal Carrier	No. of Children	No. of Parents	Adjusted* Ratio
Introducers	58	16	2·4
Spreaders	19	4	3·2
Recipients	41	10	2·7

* As each family consists of three children and two parents, each adjusted ratio equals $\frac{\text{number of children}}{3}$ divided by $\frac{\text{number of parents}}{2}$.

The connexion between the nose and throat distribution of the streptococci in the person introducing the new type and the spread of the organism to other members of the family was investigated. All 74 introducers had positive throat swabs, while 13 of them also had positive nose swabs. Six of these 13 and 17 of the 61 with negative nose swabs were spreaders. Thus, while 17 out of 23 (74%) of the spreaders had negative nose swabs, there was a higher incidence of transfers from combined nose and throat carriers than from throat carriers.

Staphylococci

Fig. 7 shows the incidence of *Staph. pyogenes* in the nose and throat swabs taken fortnightly. The main features are the predominantly nasal distribution and the higher incidence of staphylococcal nose carriers in school than in pre-school children.

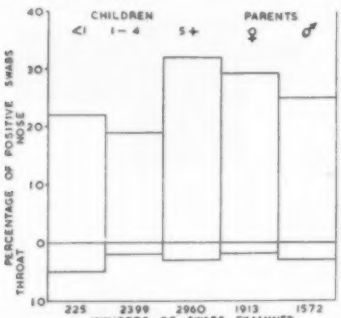


FIG. 7.—Nose and throat incidence of *Staph. pyogenes*.

The isolation rates of *Staph. pyogenes* from nose swabs taken from the frequently swabbed families were not significantly affected by nasal discharge.

Penicillin sensitivity tests were not done routinely, but, of 30 strains isolated from members of the survey during 1954, 12 were resistant to a concentration of penicillin of one unit per ml. (method of May and Morley, 1952).

Discussion on Methods

Optochin Sensitivity

During the first year of the survey most of the Gram-positive cocci showing flat or smooth colonies with green zones were tested for bile solubility, using sodium desoxycholate as described by Mackie and McCartney (1953), as well as for sensitivity to optochin. All organisms showing a zone of inhibition more than 5 mm. wide were found to be bile-soluble, and all but a few of these were typable pneumococci. The few exceptions had tiny colonies and were considered to be "rough" pneumococci. Most other colonies of Gram-positive cocci with green zones showed no zone of inhibition by the optochin strip. Both these and the few organisms showing zones of inhibition between 0 and 5 mm. were invariably bile-insoluble. However, some subcultures of pneumococci included a few colonies more resistant to optochin than the rest, although identical in appearance. Such colonies gave rise to uniformly resistant growths on subculture (zones of inhibition less than 5 mm. wide) and were shown by capsular swelling to belong to the same type as the parent strain.

The use of optochin for identifying pneumococci has been described by Bowers and Jeffries (1955), who used a disk method and a concentration of optochin of 1 in 4,000. Our results agree closely with theirs, and, like them, we consider that optochin sensitivity is a satisfactory and simple way of identifying pneumococci.

Use of Selective and Enrichment Media

In nose and throat bacteriology the mixed flora is the main difficulty in isolating individual species. Large colonies, such as those of staphylococci and *Neisseria catarrhalis*, tend to obscure small colonies, such as those of pneumococci, haemolytic streptococci, and haemophili.

CVN_2 medium contains crystal violet, which inhibits staphylococci and diphtheroids, and sodium azide, which inhibits neisseriae. The medium was used by Holmes and Lermit (1955) for the selective growth of beta-haemolytic streptococci, but its value for us was that it also enriched pneumococci, haemophili, and coliform bacilli. The concentration of azide was, at 1:16,000, less than that ultimately adopted by Holmes and Lermit because this is the maximum concentration which allows growth of haemophili. Unfortunately this concentration permits the growth of some strains of *Neisseria*, but the difficulty was overcome for the isolation of pneumococci and haemolytic streptococci by using a selective medium containing B.V.S. for subculture from CVN_2.

The use of streptomycin in a selective medium for pneumococci and streptococci was suggested to us by Dr. C. W. Morley, who had found from routine sensitivity tests (May and Morley, 1952) that pneumococci consistently grew in the presence of 5 μg. of streptomycin per ml. We found that some strains of pneumococci and haemolytic streptococci were partially inhibited by 5 μg./ml., but none by 2 μg./ml. This concentration was sufficient to inhibit almost all strains of crystal-violet-resistant neisseriae and most strains of *Haemophilus*, including many haemolytic strains which are difficult to distinguish from haemolytic streptococci. Most coliform bacilli failed to grow on B.V.S. or produced a scanty growth of small colonies, while the spreading of most strains of *Proteus* was prevented.

Discussion on Epidemiology

The seasonal variations in the incidence of the main respiratory pathogens showed interesting contrasts. Our findings that pneumococcal isolation rates were higher in the winter may be contrasted with an investigation of the nasopharyngeal flora of adults working in the London School of Hygiene (Straker *et al.*, 1939). In that investigation there were no consistent seasonable fluctuations in the isolation rates of pneumococci, although there was a distinct fall during July or August in three of the seven years of the study.

For haemolytic streptococci Straker *et al.* (1939) and Blackburn *et al.* (1930) in this country and Pike and Fashena (1946) in the U.S.A. have, like us, found no consistent seasonal trend in isolation rates; but during one or more years of each investigation, including our own, a sharp rise in the autumn has been a feature. On the other hand, Coburn and Pauli (1941), in their studies in New York City, reported a rise in isolation rates of haemolytic streptococci from throat swabs during the first quarter of the year, and a peak in the second quarter.

The isolation rates of the main respiratory pathogens according to age group showed considerable differences. For pneumococci and haemophili, children under 5 years showed the highest incidence and there was a steady reduction with age. Straker *et al.* (1939) were unable to establish this trend with age because they investigated separate communities of adults and children living under different environmental conditions.

Schoolchildren showed the highest incidence of staphylococci and group A streptococci. Cunliffe (1949), in an investigation of staphylococcal incidence in the nose, found an age distribution very similar to ours. Holmes and Williams (1954) investigated the incidence of group A streptococci in the throat swabs of children in three Middlesex boroughs. They found that children of 1 to 4 years not attending day nurseries showed a streptococcal incidence about a quarter of that of the schoolchildren, while children attending day nurseries showed a higher incidence than the schoolchildren. In our survey the children from 1 to 4 years old did not attend day nurseries but showed an incidence of group A streptococci almost as high as the schoolchildren. This finding might be due to close contacts outside the home between children under 5 years in the Paddington district compared with the Middlesex boroughs sampled by Homes and Williams, although we have no precise data on this point.

The differences in nose and throat distribution between the respiratory pathogens indicate the practical importance of choice of swab in clinical bacteriology. While a nose swab is adequate for the detection of staphylococci and a throat swab for haemolytic streptococci, both swabs should be taken for the detection of pneumococci and haemophili.

Analysis of the spread of specific types of pneumococci and group A streptococci within the survey families shows differences between the children and the adults. In the frequently swabbed families about as many new pneumococcal types appeared in the noses or throats of the parents as of the children, but the pneumococci persisted in 9 out of 10 children and only 3 out of 11 adults.

The higher pneumococcal carrier rates of children compared with adults appears from this evidence to be due not to greater exposure of children to pneumococci but to persistence of the pneumococci more often in children than in adults. The disproportionately high incidence of pneumococcal types 6, 19, 23, and 14 in the pre-school children, the age group showing the highest pneumococcal isolation rate, suggests that persistence in the upper respiratory tract of young children is a special property of these types.

A similar analysis of new types of group A streptococci in the frequently swabbed families could not be carried out, as only three new types appeared. Table IV shows that new streptococcal types were detected by the fortnightly swabbings more than twice as commonly in the children as in the adults. As new bacterial types are unlikely to be detected by infrequent swabbing unless they persist, this result is comparable with the greater frequency of persisting pneumococci in the children of the frequently swabbed families. It does not necessarily imply that the children were exposed to new streptococcal types more often than the adults.

It has been shown that nasal carriers are more likely to disseminate streptococci than throat carriers (Hamburger, Green, and Hamburger, 1945). Our figures also showed this, although 74% of the spreaders had negative nose swabs, indicating that throat carriers were numerically more important than nasal carriers in disseminating streptococci. It is noteworthy that only a third of the specific types of group A streptococci introduced into a family spread to another member, although isolation of the specific type from a member of the family continued for an average period of 10 weeks.

Figs. 2 and 5 show how nasal discharge increases the nasal isolation rates of pneumococci and haemophili. These increases might be due to (1) an increase in the number of these organisms; (2) forward extension of the area of mucous membrane in the nares colonized by them, their normal habitat being the nasopharynx; or (3) an increased incidence by acquisition from outside sources. Factor 1 would affect the isolation rate less the more efficient the method of isolation, and would account for the greater enhancing effect of enrichment in the absence of nasal discharge. Similarly, the greater enhancing effect of enrichment in the parents compared with the children suggests that pneumococci and haemophili are scantier or less accessible in the noses of adults compared with children. The contrast between the effect of nasal discharge on the normal isolation rates of the children and the adults obtained with the aid of enrichment is likely to be associated with factors 2 and 3.

Summary

Simple techniques for the isolation of the main respiratory pathogens are described and the value of optochin for the identification of pneumococci is confirmed. The use of an enrichment method consisting of incubation of the swab in crystal-violet/sodium-azide/blood-agar and subsequent streaking on selective media resulted in a 40% increase in the yield of pneumococci and non-capsulated haemophili and a doubling of the yield of group A streptococci and coliform bacilli.

The distribution of the principal respiratory pathogens in the nose and throat is given for pre-school and school-children and for mothers and fathers. Pneumococci and staphylococci predominated in the nose and haemolytic streptococci in the throat, while haemophili were evenly distributed between nose and throat. The nasal incidence of both pneumococci and haemophili showed a steady decline with age, while staphylococci and haemolytic streptococci had their highest incidence in children of school age.

Analysis of the introduction of new pneumococcal types into the frequently swabbed families indicated that the higher carrier rates of the children compared with the parents were due not to a larger number of acquisitions of new types but to a greater tendency of the pneumococci to persist in the children's noses and throats.

The fortnightly swabbings showed that an individual often carried the same type of pneumococcus, group A streptococcus, or capsulated haemophilus for months. Spread of pneumococci to other members of the families was usual with some types and unusual with others. Spread of types of group A streptococci was detected in a third of the introducers. Not only did families show considerable differences in isolation rates of respiratory pathogens, but family members often differed among themselves in the specific type of organism which they carried at any one time.

The use of the enrichment method of culture for the frequent swabbing indicated that nasal discharge was associated with a rise in nasal incidence of pneumococci and haemophili in the children but not in the parents.

We thank Dr. G. T. Stewart for his preliminary work on bacteriological methods and Professor R. Cruickshank for his advice and encouragement throughout the bacteriological work and during the preparation of the paper. We are indebted to Miss D. Allen for her invaluable technical assistance during more than a year of the survey and to Miss M. Brown and Miss V. Kirkpatrick for technical help and preliminary analysis of the data.

REFERENCES

Blackburn, R. H., Boston, R. B., Gilmore, E. St. G., Lovell, R., Wilson, S. P., and Smith, M. M. (1930). Reports on Public Health and Medical Subjects, No. 58. H.M.S.O., London.
Bowers, E. F., and Jeffries, L. R. (1955). *J. clin. Path.*, **8**, 58.
Breese, B. B., and Disney, F. A. (1956). *Pediatrics*, **17**, 834.
Brimblecombe, F. S. W., Cruickshank, R., Masters, P. L., Reid, D. D., Stewart, G. T., and Sanderson, D. (1958). *Brit. med. J.*, **1**, 119.
Coburn, A. F., and Pauli, R. H. (1941). *J. exp. Med.*, **73**, 551.
Commission on Acute Respiratory Diseases (1948). *Proc. Soc. exp. Biol. (N.Y.)*, **69**, 45.
Cunliffe, A. C. (1949). *Lancet*, **2**, 411.
Everall, P. H. (1953). *J. med. Lab. Technol.*, **11**, 181.
Fothergill, L. D., and Wright, J. (1933). *J. Immunol.*, **24**, 273.
Hamburger, M., Green, M. J., and Hamburger, V. G. (1945). *J. infect. Dis.*, **77**, 68, 96.
Holmes, M. C., and Lermit, A. (1955). *Monthly Bull. Minist. Hlth Lab. Serv.*, **14**, 97.
—— and Williams, R. E. O. (1954). *J. Hyg. (Lond.)*, **52**, 165.
Mackie, T. J., and McCartney, J. E. (1953). *Handbook of Practical Bacteriology*, 9th ed. Livingstone, Edinburgh and London.
Maxted, W. R. (1948). *Lancet*, **2**, 255.
—— (1954). *J. clin. Path.*, **6**, 224.
May, J. R., and Morley, C. W. (1952). *Lancet*, **1**, 636.
Pike, R. M. (1944). *Proc. Soc. exp. Biol. (N.Y.)*, **57**, 186.
—— and Fashena, G. J. (1946). *Amer. J. publ. Hlth*, **36**, 611.
Straker, E., Hill, A. B., and Lovell, R. (1939). Reports on Public Health and Medical Subjects, No. 90. H.M.S.O., London.

The following were the winners of prizes in the South-west Metropolitan Regional Hospital Board's 1957 competition for clinical research reports. The Board is holding a similar competition this year:

Consultants and S.H.M.O.s.—Dr. A. A. Cunningham and Dr. J. Towers, 200 guineas each. *Senior registrars, registrars, and J.H.M.O.s.*—Mr. J. C. Gazet and Dr. A. J. Taylor, 100 guineas each; Mr. P. W. Seargeant, Dr. J. R. H. Pinkerton, and Dr. P. Farnan, 75 guineas each. *Senior house officers and house officers.*—No entries.

FURTHER INVESTIGATIONS OF THE ANTIGENIC ACTIVITY OF BRITISH POLIOMYELITIS VACCINE

REPORTS TO THE MEDICAL RESEARCH COUNCIL*

A. SEROLOGICAL RESPONSE OF CHILDREN TO A THIRD DOSE OF POLIOMYELITIS VACCINE 18 MONTHS AFTER PRIMARY IMMUNIZATION

In a report to the Medical Research Council (1957b) it was shown that substantial antibody responses were obtained when a third dose of poliomyelitis vaccine was given to children 8 to 11 months after their primary immunization (Medical Research Council, 1957a). During this period of 8 to 11 months a decline in antibody levels occurred, resulting in a number of children with low titres at the time of the third dose. The question was raised whether a longer period between the primary and third doses would result in a higher proportion of children with low titres and in less substantial responses. A study was therefore made to determine the decline in antibody 18 months after primary immunization and the response at this time to a third injection of vaccine.

Procedure

Inoculation of Children.—One batch of formalin-killed vaccine was used, batch No. 12, prepared by Glaxo Laboratories from Brunenders (type 1), MEF-1 (type 2), and Saukett (type 3) strains. Twenty-one children, who took part in the early study (Medical Research Council, 1957a), and who originally had no antibodies to any of the three types of poliomyelitis virus, were given a third dose of 1 ml. of vaccine 18 months after their second dose. Fourteen were from Southend-on-Sea, four from London, and three from Scotland. The vaccine was given intramuscularly into the left deltoid, and on the same day a sample of blood was taken; a second blood sample was taken 11 to 14 days later.

Titration of Sera.—Sera were titrated for poliomyelitis-neutralizing antibodies by the method already described (Biological Standards Control Laboratory, 1957). Titres are expressed as the dilution of serum in the serum–virus mixtures before being added to cell cultures. For each child the sera taken before and after the third dose were titrated in the same test together with the serum taken two to three weeks after the second dose. In this way it was possible to make a valid comparison of antibody levels at the various stages of immunization. The values obtained from the repeat titrations of the sera taken after the second dose were similar to those obtained previously. In addition, 15 of the 21 sera taken before the first injection of vaccine were retested; these sera were originally considered triple-negative, having shown no neutralization at a dilution of 1/8. The retests were made at a dilution of 1/2 by mixing undiluted serum with an equal volume of virus suspension. None of the sera neutralized any of the three types of virus, thus confirming the earlier view that the children taking part in the study were clearly triple-negative.

Results

At the time of giving the third dose 9 of the 21 children were shown to have antibody titres to a particular type which were higher than, or equal to, the corresponding titres recorded two to three weeks after the second dose (Table I). In some cases this was no doubt due to inapparent infections occurring during the 18-months period between the second and third doses. In calculating mean titres (Table II) it was considered advisable to exclude all those sera which showed no decline in titre at the time of the third dose. All results, however, are recorded in the Figures and the titres given in Table I are shown as open circles.

TABLE I.—*Antibody Titres of Nine Children Who Showed no Fall in Titre to a Particular Type Between the Second and Third Doses of Poliomyelitis Vaccine*

Subject	Virus Type	Antibody Titre		
		After Second Dose	Before Third Dose	After Third Dose
A.B.	1	128	1,024	16,384
D.S.S.	1	256	256	16,384
	3	64	128	32,768
S.N.G.	2	256	512	4,096
C.S.	2	32	512	16,384
A.C.	2	64	256	16,384
P.K.	1	64	256	1,048,576
S.B.	1	16	1,024	16,384
	2	128	128	8,192
S.P.	2	128	256	16,384
W.R.	1	4	1,024	4,096

TABLE II.—*Geometric Mean Antibody Titres in Children After Two and Three Doses of Poliomyelitis Vaccine*

No. of Sera	Virus Type	Geometric Mean Antibody Titre		
		After Second Dose	Before Third Dose	After Third Dose
16	1	38	7	2,780
16	2	233	117	17,870
20	3	66	11	7,640

Fig. 1 shows the individual titres for each type at the three different stages during immunization. The decline in antibody titres between the second and third doses was least for type 2, which showed a fall in mean titre from 233 to 117 with none of the sera having a titre of less than 32 at the time of the third dose. With type 1 the mean titre fell from 38 to 7 and with type 3 from 66 to 11; with each of these types eight children had titres of four or less at the time of the third dose. It is also evident from Fig. 1 that the third injection of vaccine produced substantial responses to all three types. The increase in mean titre for type 1 was from 7 to 2,780, for type 2 from 117 to 17,870, and for type 3 from 11 to 7,640.

A more detailed analysis of the results is shown in Fig. 2, which gives for each child the titres before and after the third dose. It is seen that each child responded well to all three components. The response was especially striking with type 2, in which the lowest titre after the third dose was 2,048; and, although the responses to types 1 and 3 were not so great, no child showed a titre of less than 128 with either type. The results were similar to those reported previously in children who received their third dose 8 to 11 months after primary immunization (Medical Research Council, 1957b).

It is also seen from the Figures that, in those cases which had been excluded from the analysis on account of the possibility of inapparent infection, the responses to the third dose were of the same order as those of the rest of the group.

Summary

The effect of a third dose of poliomyelitis vaccine given 18 months after primary immunization was studied in a

*The Epsom College study was organized by the medical officer of the college, Dr. E. J. C. Kendall, who with the help of Drs. T. S. L. Beswick, T. W. Osborn, and J. O'H. Tobin carried out the vaccination and collection of sera. In the other studies subjects were vaccinated and the sera collected by Dr. A. M. Peach (London), Drs. Stevenson Logan and A. D. Macrae (Southend-on-Sea), Dr. R. C. MacLeod (Scotland), Professor Wilson Smith (University College Hospital), Dr. M. L. N. Willoughby (St. Mary's Hospital), and Drs. D. R. Bangham, T. S. L. Beswick, P. H. A. Sneath, and J. O'H. Tobin (National Institute for Medical Research).

Sera were titrated by Dr. F. T. Perkins and Miss R. Yetts, with the technical assistance of Miss F. A. Hill, Miss K. South, and Miss P. Tumber (Biological Standards Control Laboratory, Hampstead).

The results were analysed and the report was prepared by Dr. F. T. Perkins.

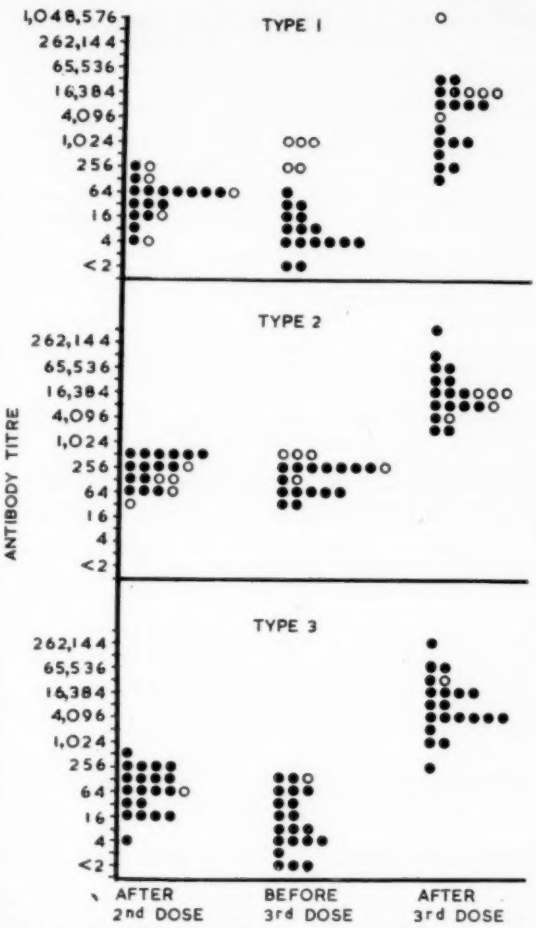


FIG. 1.—Antibody levels in children after two and three doses of poliomyelitis vaccine. Serum titres excluded from the analysis on account of the possibility of inapparent infections are shown as open circles.

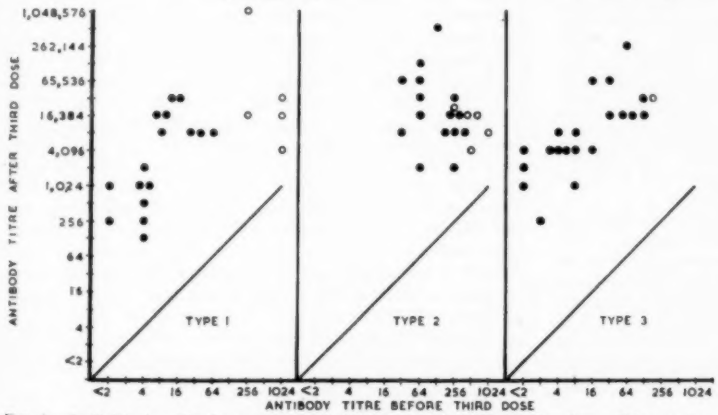


FIG. 2.—Individual antibody responses of children to a third dose of poliomyelitis vaccine. Serum titres excluded from the analysis on account of the possibility of inapparent infections are shown as open circles.

group of 21 children who originally had no antibodies to any of the three types of poliomyelitis virus.

It was shown that the children produced, to all three components of the vaccine, substantial antibody responses which

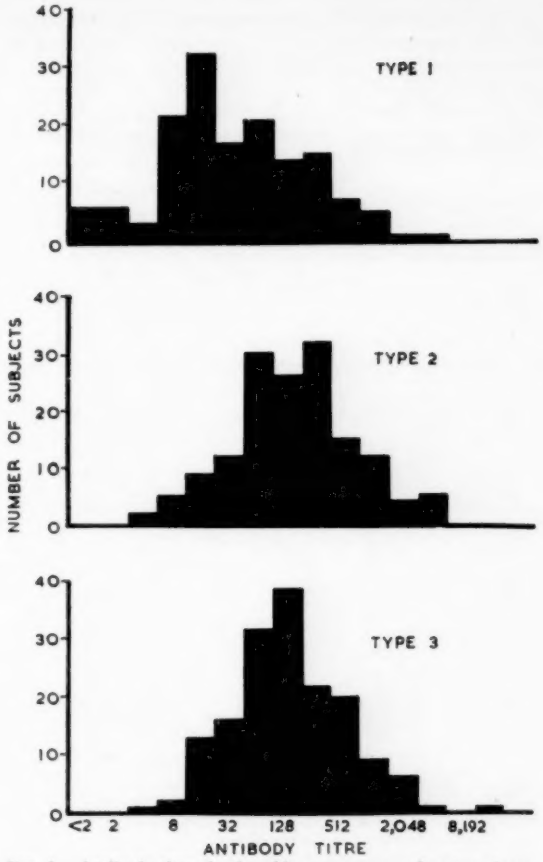


FIG. 3.—Antibody titres in the older age groups after two doses of poliomyelitis vaccine.

were similar to those produced by children who received their third dose 8 to 11 months after primary immunization.

The decline in antibody levels during the 18-months period between the primary and third doses was least in the case of type 2, and this type gave the best response to the third dose.

B. SEROLOGICAL RESPONSE OF OLDER AGE GROUPS TO TWO DOSES OF POLIOMYELITIS VACCINE

In previous studies (Medical Research Council, 1957a, 1957b) the antigenic activity of British poliomyelitis vaccine was tested in children aged 1 to 9 years. In view of the extension of the immunization programme in this country, further studies have now been made with subjects in older age groups. The subjects, whose ages ranged from 13 to 50 years, were made up of three groups—namely, schoolboys at Epsom College, medical students at University College Hospital and St. Mary's Hospital, and laboratory workers at the National Institute for Medical Research at Mill Hill and Hampstead. The tests were made only with triple-negative subjects—that is, those who had no antibodies to any of the three types of poliomyelitis virus before receiving vaccine.

TABLE III.—*Naturally Occurring Poliomyelitis Antibodies in Sera of Laboratory Workers, Medical Students, and Schoolboys*

Group (Age in Years)	No. of Sera	Number of Sera (and %) with Antibodies to:			
		No Type	One Type Only	Two Types Only	Three Types
Laboratory workers (18–50) ..	170	21 (12)	Type 1 17 ,, 2 9 ,, 3 12 } 38 (22)	Type 1+2 18 ,, 1+3 19 ,, 2+3 13 } 50 (30)	61 (36)
Medical students (20–25) ..	102	26 (26)	Type 1 12 ,, 2 13 ,, 3 5 } 30 (29)	Type 1+2 22 ,, 1+3 7 ,, 2+3 7 } 36 (35)	10 (10)
Schoolboys (13–19)	380	113 (30)	Type 1 54 ,, 2 50 ,, 3 47 } 151 (40)	Type 1+2 32 ,, 1+3 22 ,, 2+3 29 } 83 (21)	33 (9)
Totals	652	160 (25)	Type 1 83 ,, 2 72 ,, 3 64 } 219 (34)	Type 1+2 72 ,, 1+3 48 ,, 2+3 49 } 169 (25)	104 (16)

TABLE IV.—*Serological Responses of Laboratory Workers, Medical Students, and Schoolboys to Poliomyelitis Vaccine*

Group	Vaccine Batch	No. of Sera	Virus Type	Number of Sera with Antibody Titre of:														Geometric Mean Titre
				<2	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096	8,192	16,384	
Laboratory workers and medical students	6	20	1	0	0	0	3	5	4	5	0	3	0	0	0	0	0	0	36
			2	0	0	0	0	2	2	1	2	9	4	0	0	0	0	0	157
			3	0	0	0	0	3	1	5	3	4	3	1	0	0	0	0	115
	7	26	1	1	2	0	6	4	4	2	4	1	2	0	0	0	0	0	26
			2	0	0	0	0	1	1	3	4	6	4	5	0	2	0	0	292
			3	0	0	1	0	4	2	7	4	1	4	2	1	0	0	0	100
Schoolboys	10	38	1	2	1	1	7	7	3	6	6	3	1	0	1	0	0	0	31
			2	0	0	1	3	2	4	10	8	6	1	2	0	1	0	0	86
			3	0	0	0	1	1	3	8	10	8	2	2	2	0	0	1	159
	11	34	1	2	2	2	2	14	3	1	1	2	1	3	0	1	0	0	28
			2	0	0	1	2	3	3	7	7	6	1	1	2	1	0	0	102
			3	0	0	0	0	0	3	6	10	4	7	1	2	1	0	0	200
	12	34	1	1	1	1	4	3	3	7	3	6	3	2	0	0	0	0	59
			2	0	0	0	0	1	2	9	5	5	5	4	2	1	0	0	209
			3	0	0	0	1	0	2	6	12	5	4	3	1	0	0	0	164
Totals ..		152	1	6	6	4	22	33	17	21	14	15	7	5	1	1	0	0	35
			2	0	0	2	5	9	12	30	26	32	15	12	4	5	0	0	148
			3	0	0	1	2	8	11	32	39	22	20	9	6	1	0	1	149

Procedure

Vaccine and Inoculation Schedule.—Five different batches of formalin-killed vaccine (Glaxo) were used, numbered 6, 7, 10, 11, and 12. Batches 6 and 7 were used for the medical students and laboratory workers and 10, 11, and 12 for the schoolboys. Each subject received two doses intramuscularly into the left deltoid at an interval of four weeks, and a blood sample was taken two weeks after the second dose.

Titration of Sera.—Serum taken before vaccination was considered triple-negative if it was unable to neutralize, at a dilution of 1/2, any of the three types of virus. When titrations were made of the sera taken after vaccination, the corresponding sera taken before vaccination were retitrated in the same test.

Selection of Triple-negative Subjects.—In selecting subjects for the study, the sera of 652 were titrated. The results of these "screening" tests are shown in Table III, which gives, for each group of subject and for all groups combined, the distribution of naturally occurring poliomyelitis antibodies. Of the 652 tested, 160 proved to be triple-negative and were thus eligible for the study. In the remaining 492 the antibodies to the different types were fairly evenly distributed: 307 had antibodies to type 1, 297 to type 2, and 265 to type 3.

Results

Sera were obtained after vaccination from 152 of the 160 triple-negative subjects. The results of the serological responses to each of the five batches of vaccine and to all batches considered together are given in Table IV. The combined results are also shown in Fig. 3. It is evident that the responses to types 2 and 3 were decidedly better than that to type 1. All 152 subjects had titres of 4 or greater to types 2 and 3, with geometric mean values of 148 and 149 respectively. With type 1, however, 12 subjects failed to respond to a titre of 4 and the geometric mean value was 35. No attempt has yet been made to compare the antigenic activity of the different batches of vaccine; this will be the subject of a further communication in which the responses in humans will be compared with those in laboratory animals.

A broad comparison between the results obtained with the older age group and those reported previously with children aged 1 to 9 years (Medical Research Council, 1957a) suggests that the response to type 1 was not as good in the older group as in the younger one. Of the 196 in the younger group, only one failed to give a titre to type 1 of 4 or greater, compared with 12 of the 152 in the older group. The comparison is not a strict one, since different batches of vaccine, except for batch 6, were used in the two different groups. If, however, the comparison is made on the basis of the results with batch 6 only, a similar conclusion is reached, since the mean titre for type 1 in the younger group was 117 and in the older group 36. It will be possible to make a further comparison when the results of the effect of a third injection of vaccine in the older group are available.

Summary

The serological response to poliomyelitis vaccine was studied in a group of 152 subjects whose ages ranged from 13 to 50 years and who, before receiving vaccine, had no anti-

bodies to any of the three types of poliomyelitis virus. Two injections of vaccine were given at an interval of four weeks and antibody levels determined two weeks after the second dose.

Antibody titres of 4 or greater were produced by all subjects to types 2 and 3 and by all except 12 to type 1. In general the responses were similar to those previously reported in children aged 1 to 9 years, although there was some indication that the older group did not respond to type 1 as well as the younger group.

Those concerned in these studies wish to thank the Headmaster of Epsom College for his valuable co-operation and the Ministry of Health for the supply of poliomyelitis vaccine.

REFERENCES

Biological Standards Control Laboratory (1957). *Brit. med. J.*, **2**, 124.
Medical Research Council (1957a). Ibid., **1**, 366.
—— (1957b). Ibid., **2**, 1207.

VENOUS DRAINAGE OF ANTERIOR TIBIO-FIBULAR COMPARTMENT OF LEG, WITH REFERENCE TO VARICOSE VEINS

BY

N. A. GREEN, M.B., B.S., F.R.C.S.

J. D. GRIFFITHS, M.B., B.S., F.R.C.S.

AND

G. A. D. LAVY, M.B., B.Chir., F.R.C.S.

Departments of Anatomy and Surgery, St. Bartholomew's Hospital, London

The surgical treatment of varicose veins of the lower limbs at the present time usually consists of some combination of ligation, stripping, and injection of the long and short saphenous systems. Provided care is taken in the choice and use of these methods, good results are to be expected.

It early became clear that ligation of the long and short saphenous veins at the saphenous opening and in the popliteal fossa respectively would not control all cases even when combined with stripping of the main vein. Some at least of the poor results have been due to failure to appreciate and deal with incompetent perforating veins in various parts of the lower limbs, such as those described by Cockett (1955).

In examining this problem our attention has been drawn to the relatively constant pattern of the venous drainage of the superficial tissues of the anterior part of the leg—i.e., in the skin and superficial fascia overlying the anterior tibio-fibular compartment. Some of these anterior compartment veins tend to drain, independently of the long and short saphenous systems, into the deep veins of the leg. Hence superficial varicosities may be encountered in this compartment without any corresponding saphenous varicosity, although incompetence in these "perforating" veins may, by virtue of connexions with the long and short saphenous systems, give rise to recurrent varices in these veins. Such "non-saphenous" varicosity is uncommon and yields to ligation of the perforating veins where they pierce the deep fascia.

This paper both records an investigation into the anatomy of these anterior leg veins and reports the results of the treatment of varices thereof. The investigation was carried out on 19 dissecting-room legs and on three legs amputated at operation. The position and relationship of the perforating veins as they pierced the deep fascia of the anterior tibio-fibular compartment were recorded. The amputated legs were dissected after injection with latex to show the deep connexions of these anterior perforating veins.

Anatomical Details

A series of veins perforating the deep fascia investing the anterior department of the leg was found in all cases; a typical arrangement is illustrated in Fig. 1. The perforating veins varied between 4 and 10 in number and were situated in an irregular linear distribution, between 2 and 5 cm. behind the crest of the tibia. One constant vein piercing the extensor retinaculum in front of the ankle-joint has been termed the "pre-malleolar vein," and another perforating vein midway up the leg the "mid-crural vein." The remainder were scattered more or less evenly between the level of the superior tibio-fibular joint and the ankle. In the dissecting-room specimens the diameter of the perforating veins varied from about 2 mm. down to vessels little larger than thick thread.

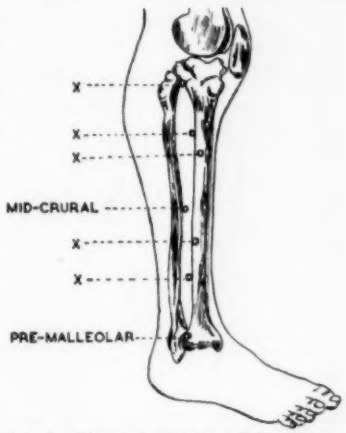


FIG. 1.—Diagram showing origins of perforating veins found on dissection in anterior tibio-fibular compartment of leg. X indicates sites of perforation of deep fascia.

The pre-malleolar vein constantly afforded communication between the superficial veins of the dorsum of the foot and the deep veins of the leg. The mid-crural vein usually had no communication with the long or short saphenous veins, but occasionally was found to anastomose with an anterior branch of the long saphenous passing over the subcutaneous border of the tibia (Fig. 2). This pre-malleolar vein is distinct from the lateral ankle-perforating vein described by Dodd and Cockett (1956), which winds around the fibula, draining into the peroneal vein. The remaining perforating veins were usually devoid of visible anastomosis with the long and short saphenous veins and appeared merely to drain localized areas of the skin.

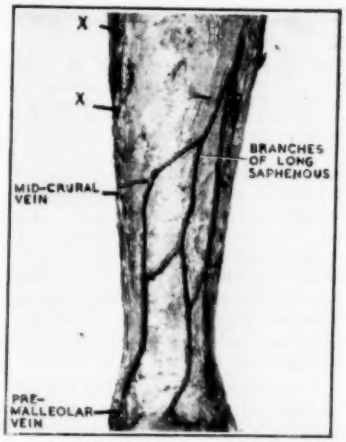


FIG. 2.—Dissection of amputated specimen, showing sites at which perforating veins pass through deep fascia.

The three amputated legs dissected after injection showed that the veins of the anterior tibio-fibular compartment drain into the venae comites of the anterior tibial artery

beneath the extensor muscles of the leg. In one dissection a communication was also noted to pass through the interosseous membrane to join a plexus of veins around the peroneal artery deep to the flexor hallucis longus. These perforating veins are subsidiary to the tributaries of the long and short saphenous veins, which are responsible for the main drainage of the compartment, and are of importance only when they become incompetent or feed an incompetent saphenous system.

Clinical Material

Varicosities of the anterior perforating veins of the leg alone are rare, but two patients have been seen in whom there was no involvement of either the long or the short saphenous systems (Fig. 3). In both patients the varicosities were not controlled by a tourniquet obliterating the long saphenous vein in the thigh or by occlusion of the short saphenous vein below the knee. The site of origin of this vein was shown on phlebography (Fig. 4) to occur in the middle third of the leg midway between the tibia and fibula —that is, the mid-crural vein described above. No connexions were visible between this vein and the saphenous systems. Ligation of the perforating vein where it pierced the deep fascia was performed in both patients with excellent results.

FIG. 3 FIG. 4 FIG. 5

FIG. 3.—Infra-red photograph of varicose veins related to anterior perforating veins. FIG. 4.—Phlebogram showing site of perforation of perforating vein (mid-crural). FIG. 5.—Phlebogram showing mid-crural perforating vein (A) communicating with a varicose branch of the short saphenous vein, and the pre-malleolar perforating vein (B) arising in tibio-fibular compartment of leg.

It is suggested that either the development of valvular incompetence in one of the anterior perforating veins leads to superficial venous dilatation in the anterior tibio-fibula compartment, or that in certain patients the veins appear to enlarge so as to form a "third" saphenous vein.

In a number of other cases varicosity of these anterior perforating veins occurred in conjunction with varicosities of the saphenous systems (as seen in Fig. 5), with consequent intercommunication. In recurrence of varicose veins following extensive ligation and stripping operations it may be that the varicosities fill from these anterior perforating veins, ligation of which would control such filling.

Ulceration on the lateral side of the leg is rare, and when it does occur is slow to heal and often breaks down. In such cases the ulceration may be due to varicose veins of the short saphenous being fed by a large mid-crural perforating vein. In other cases where there have been no varicose veins visible in the lateral side of the leg, phlebograms have shown a large pre-malleolar perforating vein in the base of the ulcer. Exploration of the ulcer, as described by Cockett (1955), with ligation of the perforating vein, has resulted in healing of ulcers which have been unhealed for many years in spite of various forms of treatment.

Treatment

Treatment of varicosities of the anterior veins, without involvement of the long or short saphenous systems, should be by ligation at the site where the vein perforates the deep fascia, followed by retrograde injection with a sclerosing agent, since stripping of these veins is not usually possible. It is advisable to perform phlebograms to determine the exact point of perforation, as the varicosities themselves are often some distance from this site, and there is no constant anatomical landmark as in the case of the long and short saphenous systems.

When occurring in association with varicosities of the saphenous systems, care must be taken to ligate the anterior communicating veins, in addition to the stripping and ligation of the main saphenous systems.

Summary

The anatomy of the venous drainage of the anterior tibio-fibular compartment is investigated in 19 dissecting-room specimens and three amputated legs. A number of constant perforating veins are described, including their connexions and communications, and their importance in the treatment of varicose veins is discussed.

Cases are reported in which varicosities have developed in these veins both independently and together with main saphenous varicosities. In successful treatment of such cases it is essential that these anterior leg veins are ligated separately.

We are indebted to Professor A. J. E. Cave for his guidance and encouragement; to Mr. C. Naunton Morgan for his help and permission to publish the result of investigations on his patients; and to the photographic and *x*-ray departments of St. Bartholomew's Hospital for the illustrations.

REFERENCES

Cockett, F. B. (1955). *Brit. J. Surg.*, **43**, 260.
Dodd, H., and Cockett, F. B. (1956). *The Pathology and Surgery of the Veins of the Lower Limb*, p. 60. Livingstone, Edinburgh.

The Supplement to the Registrar-General's Statistical Review for the years 1952 and 1953 (H.M.S.O., 11s. 6d.) analyses statistics relating to patients in mental and mental deficiency hospitals. It is more detailed analysis than on previous occasions. In the tables first admissions to mental hospitals are distinguished from subsequent admissions, and a special chapter analyses the first admissions to mental hospitals in 1949–53 of men aged 20 and over according to diagnosis on admission and occupation. Serial tables are given for the first time showing trends in admissions, discharges, and deaths in the years 1949 to 1953 and the resident populations of the hospitals at December 31 in each of these years.

SURGICAL INDUCTION FOR SUSPECTED PLACENTAL INSUFFICIENCY

BY

IAN COPE, F.R.C.S., M.R.C.O.G.
Late Registrar

AND

MORTON G. PEARSON, F.R.C.S.Ed., M.R.C.O.G.
Senior Registrar

Institute of Obstetrics and Gynaecology, Hammersmith Hospital, London

In recent years there has been a marked increase in the number of surgical inductions of labour carried out at Hammersmith Hospital. The indications for induction have been widely extended to include all cases in which continuation of pregnancy may endanger the life of the foetus.

Evidence has been accumulating that impaired uterine and placental circulation, with consequent reduction in oxygen supply to the foetus, occurs in certain circumstances. Recently it has been the policy of this department to induce labour in these circumstances, in the belief that the impairment of circulation is progressive and in the expectation that early release from this unfavourable environment will save some infants who would otherwise have perished. In pursuit of this policy more than 70% of the inductions in 1956 were carried out for post-maturity, mild hypertension, or a history of bleeding during pregnancy.

The object of this paper is to consider the value of surgical induction in these cases.

Present Series

In the six years 1951 to 1956, there were 12,047 deliveries and 999 surgical inductions of labour. During this period the induction rate rose from 2.1 to 14.6%. Table I shows the indications for induction in 1953, when the rate was 7.5%, and in 1956, when it was 14.6%. The figures of Parker (1957) and Tennent and Black (1954) have been included for comparison.

TABLE I.—*Indications for Surgical Induction*

	Hammersmith Hospital		Parker 1950–2	Tennent and Black 1950–2
	1953	1956		
Total no. of inductions	140	325	1,099	1,585
Induction rate	7·5%	14·6%	19·8%	18·3%
Hypertension, pre-eclampsia	95 (68%)	193 (59%)	41%	32%
Post-maturity	32 (23%)	48 (15%)	19%	40%
Disproportion	2 (1·5%)	22 (7%)	11%	12%
Rhesus iso-immunization	1 (1%)	14 (4%)	—	1%
Others	10 (6·5%)	48 (15%)	29%	15%

In the Hammersmith series most of the cases of hypertension and pre-eclampsia were mild and the indication for induction was suspected placental insufficiency. As a blood pressure of 120/80 has been regarded as the upper limit of normal, many cases have been included under the heading of hypertension which others might have included under the heading of post-maturity. Tennent and Black record post-maturity as the indication for induction in 40% of their cases.

One-third of the cases placed under the heading of "others" in this series were also induced for suspected placental insufficiency—for example, slight bleeding during pregnancy and twin pregnancy at term.

Method of Induction

The method of induction used was rupture of the membranes preceded by castor oil, an enema, and a bath. In most cases hindwater puncture was combined with rupture of the forewaters, but on a number of occasions one or the other method alone was employed. On six occasions labour was induced by the insertion of a soft rubber tube into the lower segment.

If labour did not ensue within 24 hours, a high vaginal swab was sent for bacteriological examination and antibiotics were given prophylactically. Until the middle of 1955, caesarean section was carried out if labour had not become established within 48 hours. Since then the period has been extended to 72 hours, and within this period an attempt has been made to bring the patient into labour with an intravenous oxytocin drip.

Is the Method Safe?

Maternal Mortality.—In this series there was one maternal death, a 2-para aged 38 who had mitral stenosis. Following an accidental haemorrhage at the 38th week, the membranes were ruptured and she was delivered by forceps nine hours later. The total blood loss was 57 oz. (1,620 ml.). She was given 1 pint (570 ml.) of dextran and 3 pints (1,700 ml.) of blood. On the second day of the puerperium she developed cardiac failure, and in spite of treatment she died on the 15th day. Permission for a post-mortem examination was refused. There was no evidence to suggest that death was attributable to the surgical induction.

Maternal Injury.—No injuries due to surgical induction were recorded during the period under review.

Maternal Morbidity.—The morbidity rate for all causes following surgical induction of labour was 9.1% compared with 5.3% for all deliveries during the same period. The criterion of morbidity employed was the Ministry of Health definition of puerperal pyrexia.* The higher morbidity rate in the induced group was associated with the higher caesarean section rate in that group—14.5% compared with the overall section rate of 5.4%. The morbidity rate associated with vaginal delivery was actually lower after induced labour than after spontaneous labour (Table II). With

TABLE II.—*Puerperal Pyrexia (Ministry of Health Standard)*

	Total No. of Cases	With Pyrexia	
		No.	%
Vaginal delivery without surgical induction	11,193	430	3·8
Vaginal delivery after surgical induction	854	28	3·3
Caesarean section without surgical induction	499	132	26·5
Caesarean section after surgical induction	145	42	28·9

prophylactic antibiotic therapy, therefore, it is apparent that the maternal risk associated with surgical induction is the increased liability to caesarean section. An increase of 9.1% in the caesarean section rate has been demonstrated in the induced group, but this figure probably exaggerates the risk, because a higher section rate would in any case be expected in the group selected for induction.

Is the Method Effective?

During the years 1952–5, A. F. Bushby (personal communication) studied the induction–delivery interval in 517 cases in this department. He found that over 75% were delivered vaginally within 48 hours. He also confirmed a previous observation made by J. C. M. Browne and

*During 1951 the old standard applied—that is, "a temperature of 100.4° F. (38° C.) or over, maintained for 24 hours or recurring during that period, in the first 21 days after delivery, but excluding the first 24 hours." During 1952–6 the new Puerperal Pyrexia Regulations (1951) definition was used—that is, "a temperature of 100.4° F. (38° C.) or over occurring at any time within 14 days after delivery."

TABLE III.—*Induction-Delivery Interval (After Bushby) 1952–5 (517 Cases). Percentage of Women Delivered Vaginally Within 48 hours.*

Method of Induction	Primigravidae	Multigravidae	Total	Total No. Induced
Rupture of fore- and hindwaters	76·3%	85%	77·5%	346
Rupture of forewaters	89·7%	93%	89·8%	86
,, ,, hindwaters	72·7%	81·8%	75·3%	85

D. Meagher (1952, unpublished data) at Hammersmith Hospital that rupture of the forewaters gave better results than rupture of the hindwaters. The combined method gave results intermediate between the two (Table III).

J. Walker (1956, personal communication) found that 85% of women induced by rupture of the membranes were in labour within 72 hours. Of the remaining 15%, a considerable number had a further prolonged delay before the onset of labour. This observation led to a change in the policy in this department, and now patients who are not in labour after 72 hours are delivered by caesarean section. Walker also confirmed Browne's (1952) observation that the induction–delivery interval was not seriously prolonged when the cervix was unripe. Comparison between primigravidae with a ripe cervix and those with an unripe cervix, in regard to the percentage in labour within 72 hours of induction, showed a difference of only 7% (Walker).

Caesarean Section

Caesarean section was carried out on 145 occasions after surgical induction during the period reviewed, an incidence of 14.5%. Table IV shows the annual increase in the number of sections carried out after induction.

Although the number of caesarean sections after surgical induction has increased, the overall caesarean section rate in the hospital has scarcely altered (Fig. 1). An attempt was made to classify the indications for caesarean section after surgical induction, but it proved impossible to dissociate failure to deliver on the one hand from the original indication for induction on the other. The indication for caesarean section was foetal distress in 28% of the cases, and one section was carried out for prolapsed cord.

Tennent and Black (1954) did not advocate routine caesarean section after 72 hours. They thought that in the hypertensive and post-mature groups they lost seven babies by this policy, but in order to save those seven they calculated that they would have had to perform 113 caesarean sections. Gibson (1952) reported a very high foetal mortality (25%) when the latent period after induction exceeded 72 hours.

Is the Method Worth While?

As a result of the increasing use of surgical induction for the indications stated, a steady reduction in the overall still-birth and neonatal death rates might have been expected. The significance of such a reduction would, of course, be modified by any marked changes in the hospital population during these years.

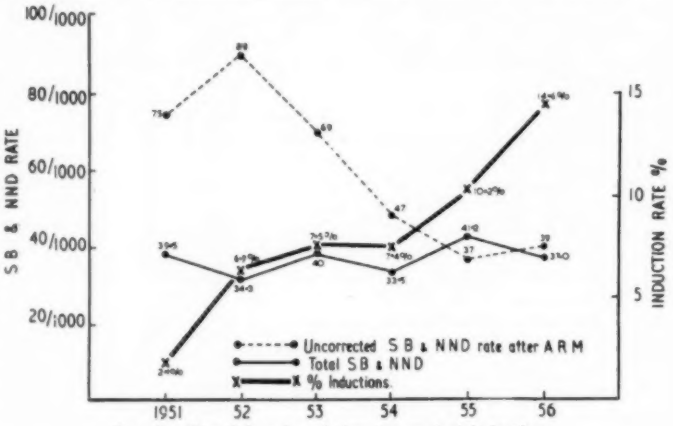


FIG. 2.—Foetal loss in relation to surgical induction.

TABLE IV.—*Caesarean Section after Surgical Induction*

	No. of Deliveries	No. of Surgical Inductions	Caesarean Section After Surgical Induction	
			No.	%
1951	1,858	40	5	12·5
1952	1,797	123	14	11·4
1953	1,921	140	16	11·4
1954	2,096	151	24	16·0
1955	2,151	220	40	18·2
1956	2,224	325	46	14·1

FIG. 1.—Surgical induction and caesarean section rates.

The hospital population has, in fact, shown little change during the six years. During 1956 the numbers of Jamaican and other coloured women increased slightly, but this group still represents less than 5% of the population. The number of unbooked admissions has always been small at this hospital, and during this period it decreased still further, from 3.5% in 1951 to 2% in 1956.

An analysis of the stillbirths and neonatal deaths into clinical groups, as suggested by Baird and Walker (1955) shows only minor changes during these years (Table V).

TABLE V.—*Grouping of Stillbirths and Neonatal Deaths Under Clinical Causes (after Baird and Walker)*

	1951–3 (All Cases)	1954–6 (All Cases)	1951–6 Induced Group
Premature, cause unknown	52	65	3
Mature, ,, ,,	21	16	4
Trauma (including stress asphyxia and cord)	24	31	5
Hypertension and pre-eclampsia	27	21	10
Ante-partum haemorrhage (without toxaemia)	24	24	6
Foetal abnormality	32	39	13
Maternal disease	3	6	2
Others—haemolytic disease	28	25	8
Total	211	227	51

The number of babies lost in the hypertension and pre-eclampsia group was seven in each of the three years 1954 to 1956 compared with an average loss of nine in the preceding three years. The "mature, cause unknown" group was reduced from seven to five. There was, however, a

corresponding increase of two in the number of deaths from trauma, stress asphyxia in labour, and cord entanglement, and an increase of three in the "premature, cause unknown" group. The number of deaths due to antepartum haemorrhage (unrelated to hypertension and pre-eclampsia) has not altered.

In the induced group a relatively large number of foetal deaths were attributed to maternal hypertension and pre-eclampsia. However, the number was no higher than would be expected as a result of the high incidence of these conditions in women who were induced.

Fig. 2 shows that the overall foetal death rate has remained virtually static, despite the marked increase in the induction rate. The combined stillbirth and neonatal death rate in the induced group fell gradually until, in 1955, it was actually lower than the total figure for all deliveries. No doubt this fall is due to the increasing number of inductions performed for minor indications; nevertheless the conditions for which induction was performed constitute a distinct danger to the baby. It may be misleading to draw any firm conclusions from this trend, but a balance sheet can be drawn up summarizing the points which have been made for and against induction.

For Induction	*Against Induction*
1. Reduction of the stillbirth and neonatal death rate in the induced group to that of the whole group.	1. Overall stillbirth and neonatal death rate has not apparently improved.
2. The overall caesarean section rate has not increased.	2. 10–15% risk of caesarean section after induction.
	3. Slightly increased morbidity rate.
	4. Psychological trauma.

Until the placental reserve can be measured, a large number of women with adequate placental function will be induced to save a few infants from placental insufficiency. A number of hospitals have reported induction rates of over 20%. They have achieved caesarean section rates after induction of under 5% by allowing the latent period to exceed 72 hours in many cases. They are thus submitting many infants to a danger far greater than that of allowing pregnancy to continue. Once surgical induction has been performed, delivery should be effected within three days.

Summary

An analysis has been made of the effect of the sevenfold increase in the rate of surgical induction of labour at Hammersmith Hospital during the period 1951 to 1956. The risk to the mother is that of caesarean section. The caesarean section rate after induction was 14.5% against an overall rate of 5.4%. Caesarean section was carried out when labour was not established within 72 hours. In spite of this policy and the rising induction rate, the overall caesarean section rate did not increase.

The incidence of puerperal pyrexia was 9.1% against the overall rate of 5.3%. This increase was entirely associated with the higher caesarean section rate.

The increased induction rate has not apparently effected a reduction in the overall foetal mortality during the period under review.

We thank Professor J. C. McClure Browne for permission to publish this material, and we are grateful to him and to Mr. Norman Morris for their helpful criticism.

REFERENCES

Baird, D., and Walker, J. (1955). *British Obstetric Practice*, p. 862. Heinemann, London.
Browne, J. C. McClure (1952). *Proc. roy. Soc. Med.*, **45**, 532.
Gibson, G. B. (1952). *J. Obstet. Gynaec. Brit. Emp.*, **59**, 814.
Parker, R. B. (1957). Ibid., **64**, 94.
Tennent, R. A., and Black, M. D. (1954). *Brit. med. J.*, **2**, 833.

TUBELESS GASTRIC ANALYSIS

BY

M. A. DENBOROUGH, D.Phil., M.B., Ch.B.

F. P. RETIEF, M.B., Ch.B.

AND

L. J. WITTS, M.D., F.R.C.P.

Nuffield Department of Clinical Medicine, the Radcliffe Infirmary, Oxford

Gastric test-meal examinations are now carried out mainly for two purposes. One is to see whether the patient is capable of secreting free hydrochloric acid, as in the diagnosis of pernicious anaemia and carcinoma of the stomach. The other is to see whether the patient secretes free hydrochloric acid in excessive amounts or concentrations, as in the study of duodenal ulcer and stomal ulceration. Segal *et al.* (1950a, 1950b) introduced a method of tubeless gastric analysis depending on the use of cation exchange resins which are dissociated in the presence of free hydrogen ions in the stomach, so that the cation is absorbed and appears in the urine. Two compounds have been used, both marketed under the trade name "diagnex." Quininium is used as the exchange cation in the one method, and the dye azure A in the other. This paper reports our results with the quininium and azure A resins used as screening tests for achlorhydria. We have compared the results with those of histamine test meals on the same patients.

Patients Studied.—We investigated 124 patients. The majority were in-patients requiring gastric analysis who had been admitted to the Radcliffe Infirmary under the care of one of us (L. J. W.). The remainder had diagnex tests as out-patients and were admitted to hospital for the histamine meal, usually for one morning only. In the latter group there was a high incidence of achlorhydria, since the patients were being investigated as part of a study of the relation between achlorhydria and anaemia.

Procedure of Diagnex Tests

The basis of the two tests is similar. The patient is requested to fast overnight for at least eight hours. He then empties his bladder, discards the urine, and takes a capsule containing caffeine sodium benzoate, 500 mg., as gastric stimulant. One hour later he again empties his bladder, this time saving the urine as a control sample. Immediately afterwards he takes 2 g. of granules by mouth—a carbacrylic cation exchange resin, "amberlite RXE-96," in reversible combination with either quininium or the orthoquinoid salt of azure A. Free hydrogen ions in the stomach liberate quininium or azure A, which is then absorbed into the blood stream and excreted in the urine. Maximum excretion normally occurs within two hours. The total urine passed in the two hours after the granules have been taken is analysed for its content of quininium or azure A.

The time limit of two hours is imposed to avoid errors due to later displacement of the test cation in the intestine by cations such as magnesium, sodium, or potassium. Drugs such as kaolin, alkalis, barium, and magnesium salts should for the same reason not be taken for 24 hours before the test.

Methods of Estimation

Urinary quininium is estimated by an ether/sulphuric acid extraction method (Kelsey and Geiling, 1942). The control urine serves as a check on any extraneous fluorescent substances present. The urine specimens are made alkaline and

diluted with distilled water to 300 ml.; 120 ml. of this is extracted with 60 ml. of anaesthetic ether; 32.8 ml. of the ether layer, which contains the quininium, is separated off and fluorescence developed by shaking well with 20 ml. of N/10 sulphuric acid. The quininium is then estimated quantitatively in a suitable fluorimeter. We used a Hilger spectrophotometer. Previous workers (Segal *et al.*, 1950b; Shay *et al.*, 1954) have shown that the presence of 15 μg. or less of quininium indicates achlorhydria, whereas more than 25 μg. indicates "free acid." Intermediate values were reported as "low free acid," and in these cases tests were repeated if possible.

In the *azure A method* the test urine is again diluted to 300 ml. with distilled water, and its colour compared with two known dye standards, supplied by the manufacturers, representing 0.3 mg. and 0.6 mg. of azure A per 300 ml. Previous *in vivo* and *in vitro* (Segal *et al.*, 1955; Sievers and Gieselman, 1956) studies have suggested that a test-urine colour more intense than the 0.6 mg. standard indicates the presence of "free gastric acid," while a colour less intense than the 0.3 mg. standard indicates achlorhydria. Intermediate values are, as in the quininium test, considered to indicate "low free acid." If the colour is less intense than the 0.3 mg. standard the specimen is acidified (one drop of 6 N hydrochloric acid per 100 ml.), placed in a boiling water-bath for 10 minutes, and allowed to cool for one hour. It is then again compared with the standards. Boiling will liberate dye from a colourless conjugated form often present in urine. We used a simple comparator block and placed the control urine behind the dye standard to compensate for the greenish hue produced by urochromes.

Tests Used for Comparison.—The quininium resin test was checked against the single-dose histamine test meal. A Ryle tube was passed and the resting juice aspirated. "Free acid" was titrated in the conventional way with Töpfer's reagent as indicator. If "free acid" was detected there was no need to go any further. If "free acid" was absent 0.5 mg. of histamine acid phosphate was injected subcutaneously and the stomach aspirated completely every 15 minutes for one hour. Later in the series the augmented histamine test meal (Kay, 1953) was introduced to check the azure A test. Histamine, 0.4 mg. per 10 kg. body weight subcutaneously, was used as gastric stimulant and covered by an antihistaminic drug (mepyramine hydrogen maleate, 100 mg. intramuscularly) to counteract the systemic effects. The gastric contents were aspirated continuously for three successive 15-minute intervals.

Results

In 73 subjects quininium resin tests and single-dose histamine test meals were performed (Table I). Good correlation between the tests was evident, disagreement occurring in only two out of the 73 cases. In three patients equivocal "low free acid" results were obtained.

TABLE I.—*Comparison of Quininium Test with Single-dose Histamine Test*

Quininium Excreted	Single-dose Histamine Test		Total
	Free HCl	No HCl	
>25 μg.	29	1	30
15–25 ,,	2	1	3
<15 ,,	1	39	40
Total	32	41	73

TABLE II.—*Comparison of Azure-A Test with Augmented Histamine Test*

Azure A Excreted	Augmented Histamine Test		Total
	Free HCl	No HCl	
>0·6 mg.	6	2	8
0·3–0·6 ,,	6	8	14
<0·3 ,,	3	26	29
Total	15	36	51

Fifty-one patients underwent the azure A test and an augmented histamine test meal (Table II). It was found that of 15 patients with "free" hydrochloric acid in the gastric juice, three were missed by the azure A method; and of 36 cases with no "free acid" two were misdiagnosed by the latter method. One patient with undoubted pernicious anaemia gave a positive result in the azure A test, though the presence of achlorhydria was confirmed by the histamine test meal. In 14 patients equivocal results were obtained—six in the free acid group and eight among the achlorhydrics.

Discussion

Segal and Miller (1955) summarized the available literature on exchange-resin gastric analysis and reported as follows: (1) Quininium method: nine false negatives among 832 patients with proved "free gastric acid" on test meal and 12 false positive among 285 patients with achlorhydria. (2) Azure A method: two false negatives among 208 patients with "free acid" and two false positives among 57 achlorhydrics.

Since then literature, on the azure A method in particular, has accumulated (Goldbloom *et al.*, 1955; Sievers and Gieselman, 1956; Sievers and Fischer, 1957; Poliner *et al.*, 1957; Bolt *et al.*, 1957; Fentress and Sandweiss, 1957; Rechtshaffen *et al.*, 1957; etc.). Among 412 patients investigated with this test, 95 were achlorhydric on intubation and there was agreement with the dye test in all but two subjects. In 317 patients with "free gastric acid" on intubation, the azure A test gave a false-negative result in 43 instances. However, it should be noted that the percentage disagreement varies widely in the different series—for example, Poliner *et al.* (1957) report the high incidence of 75% false-negative results, while Goldbloom *et al.* (1955), at the other extreme, noted a 100% agreement between dye test and intubation results.

An occasional false negative is not of much consequence if these methods are used as screening tests for achlorhydria. Subsequent gastric analysis will reveal that "free acid" is in fact being secreted. The likeliest cause of a result of this kind is inefficient gastric stimulation by caffeine benzoate. However, Poliner *et al.* (1957) have pointed out that certain pathological conditions are apt to give negative resin-test results, whatever the gastric secretion. Pyloro-duodenal obstruction, malabsorption syndromes, and severe diarrhoea may lead to defective cation absorption. Renal disease, bladder-neck obstruction, and possibly liver disease may lead to delayed excretion; few data have been published on this aspect of the subject (Behr and Lawrie, 1955; Bolt *et al.*, 1957).

If the aim is to detect achlorhydria, false positives will invalidate the test. Fluorescent substances in the urine, notably found after riboflavine or nicotinic acid has been taken by mouth, are a theoretical cause of incorrect results with the quininium method. In practice, routine analysis of the control urine obviates this difficulty. Strong cation displacers like magnesium, iron, aluminium, barium, calcium, and kaolin should not be taken by mouth for two days before the test.

Gastric operations may affect the results in various ways (Galambos and Kirsner, 1955; Poliner *et al.*, 1957). Resin granules may pass through the stomach remnant so rapidly that proper cation exchange is not possible. Alkaline intestinal juice regurgitating through an operation stoma may neutralize gastric acid. Abnormally rapid gastric emptying may result in premature liberation of dye or quininium by intestinal cations.

Our own findings with the quininium resin revealed satisfactory correlation with the single-dose histamine meal, comparable with the findings of other workers (Segal *et al.*, 1955). The azure A method, on the other hand,

although simpler to perform, has given too many equivocal results to be satisfactory. It has also given more false positives and false negatives than the quininium test. It is true that we checked it against the much more stringent augmented histamine test, but this would not explain the false positives.

There is evidence that if tubeless gastric analysis is repeated in cases in which an equivocal result has been obtained, a definitive result may be obtained in the second test (Flood *et al.*, 1953; Galambos and Kirsner, 1955; Sievers and Gieselman, 1956). It has also been suggested that histamine should replace caffeine benzoate as the gastric stimulant in tubeless gastric analysis. Indeed, Galambos and Kirsner (1955) found only one false positive and one false negative among 104 patients using betazole hydrochloride ("histalog") instead of caffeine in the azure A test. We are, however, interested in a simple test for achlorhydria which can be performed at home by the patient, and the introduction of parenteral histamine would take tubeless gastric analysis out of the category of screening tests.

The exchange-resin methods have no value as quantitative tests of gastric acidity, as the amounts of cation displaced from the resin, absorbed from the intestine, and excreted in the urine are not directly proportional to the amount of hydrochloric acid secreted by the stomach (Segal *et al.*, 1955; Galambos and Kirsner, 1955; Sievers and Gieselman, 1956). The resins are therefore of little use in the study of hyperchlorhydria and peptic ulceration. Their role is in the detection of diseases associated with achlorhydria, such as pernicious anaemia and gastric carcinoma.

Summary

The literature on tubeless gastric analysis is briefly reviewed and the circumstances under which such tests are likely to be unreliable are mentioned.

The quininium resin test was compared with the single-dose histamine test meal in the recognition of achlorhydria; agreement was satisfactory.

The azure A resin was compared with the augmented histamine test. The results were unsatisfactory, as there was too high a proportion of equivocal results. In addition, false positive and false negatives were more frequent than in the quininium test.

The quininium test is a valuable method of screening patients for achlorhydria, but the azure A method, although simpler to perform, cannot be recommended.

We thank Dr. Sheila Callender for her help and Mrs. Allison Jones and Miss Sandra Reynolds for technical assistance. We are grateful to Messrs. E. R. Squibb and Sons, Ltd., for putting the exchange resins at our disposal.

REFERENCES

Behr, G., and Lawrie, H. (1955). *Gastroenterology*, **28**, 409.
Bolt, R. J., Ossius, T. G., and Pollard, H. M. (1957). Ibid., **32**, 34.
Fentress, V., and Sandweiss, D. J. (1957). *J. Amer. med Ass.*, **165**, 21.
Flood, C. A., Jones, B., Rotton, W. M., and Schwarz, H. (1953). *Gastroenterology*, **23**, 607.
Galambos, J. T., and Kirsner, J. B. (1955). *A.M.A. Arch. intern. Med.*, **96**, 752.
Goldbloom, A. A., Feinstein, M. A., and Eiber, H. B. (1955). *Amer. J. dig. Dis.*, **22**, 288.
Kay, A. W. (1953). *Brit. med. J.*, **2**, 77.
Kelsey, F. E., and Gelling, E. M. K. (1942). *J. Pharmacol. exp. Ther.*, **75**, 183.
Poliner, I. J., Hayes, M. A., and Spiro, H. M. (1957). *New Engl. J. Med.*, **356**, 1051.
Rechtshaffen, J. S., Venet, L., and Weingarten, M. (1957). *J. Amer. med. Ass.*, **164**, 1467.
Segal, H. L., and Miller, L. L. (1955). *Gastroenterology*, **29**, 633.
—— —— and Morton, J. J. (1950a). *Proc. Soc. exp. Biol. (N.Y.)*, **74**, 218.
—— —— —— and Young, H. Y. (1950b). *Gastroenterology*, **16**, 380.
—— —— and Plumb, E. J. (1955). Ibid., **28**, 402.
Shay, H., Ostrove, R., and Siplet, H. (1954). *J. Amer. med. Ass.*, **156**, 224.
Sievers, M. L., and Fischer, G. L. (1957). *Amer. J. dig. Dis.*, **2**, 363.
—— and Gieselman, R. V. (1956). Ibid., **1**, 241.

A NEW EXAMPLE OF THE Rh ANTIBODY, ANTI-C^x

BY

GERTRUDE PLAUT, M.D.

P. B. BOOTH, M.R.C.S., L.R.C.P.

North London Blood Transfusion Centre

CAROLYN M. GILES, B.Sc.

AND

A. E. MOURANT, D.M., M.R.C.P.

Blood Group Reference Laboratory

This paper records the finding and investigation of the rare antibody, anti-C^x, in the serum of a patient and the investigation of a number of persons who were thereby shown to carry the corresponding antigen.

Present Investigation

The patient, Mrs. T., was born in 1911; she had two children, born in 1938 and 1940. The first of these died at the age of 1 week from a cause which it is now almost impossible to ascertain owing to the lapse of time. There is no record of any other pregnancy, of any transfusion, or of any injection of blood prior to the test in which the abnormal antibody was discovered.

In January, 1957, the patient was found to have an adenocarcinoma of the caecum, and was admitted for operation to the Hospital of St. John and St. Elizabeth, London. As it was anticipated that a blood transfusion would be needed she was grouped, and found to be group O, Rh(D) positive; two bottles of group O, Rh-positive packed cells (each from two donors) were then tested for compatibility with her serum. One bottle was found to be incompatible both by saline and by albumin tests. Further tests with her serum showed no agglutination of 13 other donor samples examined, or of seven samples from the transfusion centre staff, selected as covering a wide range of antigens. In all, blood from 11 donors was transfused uneventfully. The two donors who had contributed to the incompatible bottle of packed cells were recalled for further investigation.

At the Blood Group Reference Laboratory the patient's serum was tested against red cells from both these donors and from a selected panel of 22 other bloods, including known examples of the antigens Wr^a, Mi^a, V^w, and one other "family" antigen, so far unpublished. Tests were carried out in saline and albumin at 37°, 18°, and 4° C., and by the indirect anti-human-globulin method; the serum was also tested by Löw's method with cystein-activated papain, and against trypsin-treated cells. All the results were negative except in the case of the blood from one of the two contributors to the incompatible bottle, Mrs. W., which reacted in all the tests except at 4° C. in saline.

The red cells of this donor's father and sister, but not those of her mother, were also found to be agglutinated by the serum; those of the patient herself, her husband, and her surviving son were unagglutinated.

The cells of the donor, Mrs. W., were grouped as fully as possible with available standard sera. They were tested also with reagents for the antigens Wr^a, Mi^a, V^w, V, Diego, C^x, E^w, f, Be^a, R$_m$, U, Vel, and Tj^a, and for two other rare "family" antigens at present under investigation, and were found to react only with anti-C^x, anti-U, anti-Vel, and anti-Tj^a, the last three of which react with nearly all known bloods. This result strongly suggested that the patient's antibody was anti-C^x. Through the kindness of Dr. F. Stratton, who had supplied the known anti-C^x used in the tests, we received a sample of known C^x-positive

blood. This was found to react with the patient's serum. The two relatives of Mrs. W. whose cells had been found to give positive reactions with the patient's serum were also found to be C^x-positive; as described below, the red cells of an unrelated person whose cells had previously given anomalous results with anti-C sera were also tested, and they too were found to react both with the original anti-C^x and with the patient's serum.

It was now abundantly clear that the patient's serum contained anti-C^x, and that the donor Mrs. W., her father, and her sister carried the antigen C^x.

On the assumption, later confirmed, that the anti-C serum used in the full grouping of all the bloods reacted also with the C^x antigen, it was possible to deduce the C-C^x-c genotypes and, with a high degree of probability, the full Rh genotypes of the donor and members of her family. These are shown, together with the rest of their blood groups and those of the patient and her husband and son, in Table I. Three sisters and one brother of the patient were also fully tested: all proved to be C^x-negative.

A panel of 25 different anti-C sera was tested against blood specimens containing combinations of the antigens C, C^w, C^x, and c, as well as against two bloods known to contain C variants. One of these was at once found to be C^x (with c), while the other remains unclassified (see Tables II and III). All the C^{x}c bloods gave nearly identical patterns of positive and negative results, which differed from those given by C^{w}c and by the other variant; the few differences between the C^{x}c bloods are probably due to the greater age of some of the samples. Some anti-C sera were shown to contain both anti-C^w and anti-C^x, others to contain one or the other, and some to contain neither. Four pure anti-C^w sera, supposedly free from other antibodies, were tested against a variety of cells containing the C^x antigen, and were thereby shown to be free from anti-C^x. Four anti-c sera were tested against C^{x}C cells and also shown to be free from anti-C^x (see Table III).

Titration of one blood of genotype C^{x}C and one of genotype C^{x}c against anti-C^x serum showed that the C^x antigen reacts equally well in the presence of C or of c; it is not detectably depressed by the presence of C.

In order to determine the optimal conditions for agglutination by the patient's serum, it was titrated against C^x-positive cells at 37° and 18° C. in saline and in albumin, and at 37° C. with papainized cells. In all cases titres were highest at 37° C., the titres being 2 in saline, 16 in albumin, and 32 with papainized cells. The indirect anti-human-globulin technique gave relatively poor results.

Discussion

Stratton and Renton (1954) showed very clearly that the antigen C^x was the product of a gene belonging to the CC^{w}c set of alleles of the Rh series. The genetics of the family of Mrs. W. support this conclusion, as do our observations of the reactions given by the various anti-C sera with C^x-positive cells.

As it was assumed that the antibody arose spontaneously and not as a result of immunization, the sera of three brothers and one sister of the patient (all, as mentioned above, C^x-negative) were tested for anti-C^x, with uniformly negative results.

TABLE I.—*Blood Groups of Patient, Donor, and Relatives of both*

	ABO	Rh	MN	S	P	Lu^a	K	Le^a	Le^b	Fy^a
Mrs. T. (patient) ..	O CcDee	CDe cde	MN	–	–	+	–	–	+	–
Mr. T. (husband) ..	A_2B CcDee	CDe cde	MN	–	–	–	–	–	?+	+
Mr. T. (son) ..	B ccddee	cde cde	N	–	–	–	–	+	–	+
Mrs. W. (donor)* ..	O C^{x}CDeeFF	C^{x}DeF CDeF	M	+	+ + +	+	–	–	+	+
Mr. C. (father) ..	A_1 C^{x}cDee	C^{x}De cde	MN	+	+ + +	+	–	–	+	+
Mrs. C. (mother) ..	O CCDee	CDe CDe	M	–	+ +	+	–	+	–	–
Miss C. (sister)* ..	O C^{x}CDeeFF	C^{x}DeF CDeF	MN	–	+ + +	+	–	–	–	+

* Samples from these two persons only were tested with anti-f.

TABLE II.—*Reactions of Red Cells of Various C Locus Genotypes with a Panel of Saline Agglutinating Anti-C Sera**

(The scoring of reactions is that recommended in M.R.C. Memorandum No. 27)

Cells:	Ain	Bas	Hig	Joh	Lit	Log	MgB	MgN	Pea	Scr	Shr	Shw	Sh452	Sh549	Sh655	Sh800	Wat	Wel
†Cc	+ + +	+ + +	+ + +	+ +	+ + +	+ + +	+ + +	+ + +	+ +	+ + +	+	+ + +	+ + +	+ + +	+ + +	(+)	+ + +	+ + +
cc	–	–		–	–	–	–	–	–	–	–	–	–	–	–	–	–	
E.B. C^{x}c		+ + +	+ + +	+	+ + +	+	–	–		+ + +	–	+	+ +	w	+ + +	–		+ + +
Gsm.C^{w}c		+ + +		w	w	w	+ +	?	–	+ + +	w	+ + +	w	+ + +	+ + +	–		+ + +
Miss Ch. C^{x}C ..	+ + +	+ + +		+ +	+ + +	+ + +	+ + +	+ + +	+ +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+	+ + +	+ + +
Mr. Ch. C^{x}c ..	–	w		–	+ + +	w	–	w	–	+ + +	+ + +	+ + +	–	+ + +	+ + +	–	–	+ + +
‡Miss H. C^{x}c ..	–	–		–	+ + +	–	–	w	–	+ + +	+	–	–	+ + +	+ + +	–	–	+ + +
Miss E. C^{x}c ..		w			+ + +	–	–	w	–		w		+ +	+ +		–		
Mrs. W. C^{x}C ..	+ +	+ + +	+ + +	+ +		+ + +				+ + +	+ + +	+ + +			+ + +		(+)	+ + +

* Mostly containing "incomplete" anti-D as well. † The Cc control was of phenotype CcDee in all cases but two (Ain and Wat), for which it was Ccddee.
‡ Frozen cell sample only.

TABLE III.—*Reactions of Red Cells of Various C Locus Genotypes with a Panel of Anti-C Sera Free From "Incomplete" Anti-D and with Anti-C^w, Anti-C^x, and Anti-c sera*

	All with Papain														Saline		With Papain		
	Pure Anti-C							Anti-C^w				Anti-C^x			Anti-c		Anti-c		
	Bra	Bio	Cas	Fra	Gor	Sh800	Su740	Ams	Sid	BGRL	Kno	Tro	Mer		Har	Sh692	Sh720	New	Wig
R.D. Cc ..	+ + +	+ + +	+	+ + +	+ + +	+ + +	+	–	–	–	–	–	–	Cc	+ + +	+	w	+	+
Wat. cc ..	–	–	–	–	–	–	–	–	–	–	–	–	–	CC	–	–	–	–	–
E.B. C^{x}c ..	+ + +	+ + +	–	w	–	+ + +	–		–	–	–	–		Miss Ch. C^{x}C	–	–	–	–	–
Gsm. C^{w}c	(+)	+ + +	+ +	–	+ + +	+ + +	–	+ + +	+	+ + +	+ + +	–		Mrs. W. C^{x}C	–	–	–	–	–
Miss Ch. C^{x}C	+ + +	+ + +	+ +	+ + +	+ + +	+ + +	+ +	–	–	–	–	+ + +	+ + +						
Mr. Ch. C^{x}c	w	+ + +	w	–	+ + +	+ + +	+	–	–	–	–	+ + +	+ + +						
*Miss H. C^{x}c	–	+ + +	w	–	+ +	+ + +	(+)	–	–	–	–	+ + +	+ + +						
Miss E. C^{x}c	w		w	–	w		–					+ + +	+ + +						
Mrs. W. C^{x}C												+ + +	+ + +						

* Frozen cell sample only.

An outstanding problem in the present case is the source of any immunization that may have occurred. The original antibody of Stratton and Renton resulted, like most known antibodies to antigens of the Rh series, from a straightforward immunization by a foetus which was subsequently born with haemolytic disease. In the present case the husband and surviving child lack the antigen; careful questioning has revealed no history of transfusion or injection of blood before the discovery of the antibody, or of any pregnancy by anyone but the husband. A spontaneous antibody would probably, however, unlike the present one, react better at 18° C. than at 37° C. and would not be greatly enhanced by albumin; a strong indirect anti-human-globulin test would, on the other hand, have been anticipated for an immune antibody.

One further piece of evidence that may have a bearing on the origin of the antibody is given by the serum Ga, which was discovered some years ago by Dr. M. M. Pickles and was at first thought to contain only anti-S. A recent investigation by Dr. R. R. Race shows that this serum also contains anti-C^x and anti-Mi^a. It is no longer possible to investigate the antigenic stimuli which may have given rise to these antibodies, but it may be that these two antibodies to rare antigens are, like anti-Wr^a, apt to arise without specific antigenic stimuli. We are indebted to Dr. Race for allowing us to mention these unpublished facts, which incidentally make the serum described in this paper the third example, not the second, of anti-C^x to be discovered.

The serum of Mrs. T. at first appeared to contain no abnormal antibody other than anti-C^x, but after the present paper had been written it was found to contain also an antibody against a rare antigen, possibly new, at present under investigation by Dr. M. Lauer, of Hamburg, and the staff of the Blood Group Reference Laboratory. A second serum containing the same antibody was found not to react with the cells of Mr. T. nor with those of three C^x-positives, including Mrs. W. In view of this finding it should be stated that all diagnoses of the C^x antigen mentioned in this paper were confirmed with the original anti-C^x serum of Stratton and Renton, which was shown not to contain the extra antibody

Summary

A third example of the antibody anti-C^x is described, detected in the serum of an untransfused female patient in the course of compatibility tests performed prior to transfusion during surgical treatment for adenocarcinoma of the caecum. Details are given of serological tests on the red cells of the donor of the blood shown to be incompatible, and her family, together with those of comparative tests carried out with cells having a range of variants at the C locus (C, C^w, C^x, and c) and the corresponding antisera.

No source of immunization by pregnancy or injection of blood was established, and the antibody, despite some immune characteristics, was thought to be naturally occurring.

Our thanks are due to Dr. F. Kellett* and Mr. J. Clarke for their kind assistance and advice, and to Mr. D. K. Mulvany, the surgeon in charge of the case, for permission to investigate his patient.

REFERENCE

Stratton, F., and Renton, P. H. (1954). *Brit. med. J.*, **1**, 962.

*Since this paper was written we have learned with deep regret of Dr. Kellett's sudden death on February 27, 1958.

Diabetes is the subject of the fifth *Conquest Pamphlet* issued by the Research Defence Society. The pamphlet answers in simple language common questions about the disease. Copies are obtainable from the society, 11, Chandos Street, Cavendish Square, London, W.1, price 6d. each.

MULTIPLE HETEROTOPIC SQUAMOUS-CELL CARCINOMAS

A CASE REPORT

BY

J. H. EVANS, M.D., M.R.C.P.

Medical Registrar, Royal Free Hospital, London

AND

A. POMERANCE, M.B., B.S.

Registrar, Department of Pathology, Royal Free Hospital, London

The purpose of this report is to record the occurrence in one patient of three heterotopic primary squamous-cell carcinomas and to discuss the case history in relation to modern views on multiple primary tumour formation.

Case Report

The patient, a housewife, was aged 71 years at the time of her death in April, 1957. Her father had died at the age of 70 of "cancer of the lung," but there was no other history of cancer in the family. The patient had never smoked more than two or three cigarettes a day, her alcohol consumption was negligible, and she had not lived abroad. Bilateral inguinal herniae were repaired when she was 50 years old. Since about this age she had had a winter cough productive of mucoid sputum, and this had always cleared up during the summer. She had had no other illnesses, and had received no radiotherapy until the appearance of her first carcinoma.

In August, 1948, she developed a nodule on the bridge of her nose. Shortly afterwards it ulcerated and she also noticed enlarged glands in the left side of her neck. She attended hospital four weeks after the appearance of the lesion. On examination she had koilonychia but no evidence of anaemia. On the skin of the bridge of the nose there was a circular ulcer a little less than 1 cm. in diameter, with raised firm edges; it was mobile over the deep structures, and lay just to the left of the midline. Two firm discrete lymph nodes in the upper left cervical group and the left pre-auricular lymph node were palpable. There was no other abnormal finding, and, in particular, the vocal cords were normal. Examination of the blood and urine showed no abnormality. Biopsy of the edge of the ulcer showed a moderately well differentiated squamous-cell carcinoma.

The lesion healed rapidly after superficial radiotherapy to a surface dose of 6,000 r at 90 kV applied over two weeks. The enlarged lymph nodes were removed by block dissection. No metastatic deposits were seen on microscopy of the excised nodes. The neck was therefore not irradiated.

In April, 1953, the patient complained of hoarseness of the voice of five months' duration. On indirect laryngoscopy the anterior part of the edge of the left vocal cord was slightly thickened. The epithelium was intact, the cords were mobile, but there were no enlarged cervical lymph nodes. The rest of the upper respiratory tract and the other systems were normal. The skin of the nose had healed. The blood Wassermann and Kahn reactions were negative. A radiograph of the paranasal air sinuses was normal. A chest radiograph showed bilateral apical pleural thickening and calcified foci in the right cardiophrenic, right hilar, and right paratracheal regions, but there was no evidence of recent or active pulmonary disease.

Over the next three months the lesion on the vocal cord was observed at frequent intervals, and it developed into a reddish sessile swelling on the anterior third of the left vocal cord. It did not ulcerate, and the cords remained mobile. Microscopy of tissue obtained by biopsy of this

swelling in June, 1953, showed a keratinizing squamous-cell carcinoma. In August the patient received teleradiotherapy to a tumour dose of 6,925 r over six weeks. In November her voice had improved and the vocal cords had healed, leaving a small white patch at the site of the carcinoma.

She remained well, apart from her winter cough, until February, 1957, when she was brought to the out-patient department because she had become slow in speech and movement, forgetful, and at times disorientated. On questioning she had had a cough with mucoid sputum, but no haemoptysis, for a few months, and she had had a vague continuous pain in the interscapular region for the previous two weeks. Her temperature was 96.2° F. (35.7° C.), and the pulse rate was 68 a minute and regular. She was slow-witted, but she could give a history and co-operate in the examination. No other abnormality was found and there was no recurrence of either of her previous carcinomas.

Three days later she was admitted to the ward, and on the day after admission complained of weakness in her left hand. Over the next week she developed a left hemiparesis with sensory loss of a cortical type in the left limbs. Nothing abnormal was found on examination of the chest, but a radiograph showed a large circular shadow behind the heart on the left side, and a smaller opacity in the left paratracheal region. Apart from an increased E.S.R. and an excess of protein in the cerebrospinal fluid, the results of laboratory investigation were not abnormal. The patient slowly became more drowsy and disorientated. She died in coma on April 22, 1957.

At necropsy (68 hours after death) there was no evidence of recurrence of the facial or laryngeal tumours. In the lungs terminal bronchitis was present and there were bilateral apical fibrous scars. The left lower lobe was almost replaced by necrotic neoplastic tissue, which appeared to originate in the left lower lobe bronchus. The mediastinal lymph nodes were greatly enlarged by secondary neoplastic tissue. A large metastatic deposit occupied the right temporo-parietal region, and a smaller one was present in the left occipital lobe. A benign polyp was found in the rectum, and there was a small benign endometrial polyp. There were no other significant abnormalities in any system.

Histology of the left lung revealed a poorly differentiated bronchogenic carcinoma of squamous type, with marked cellular and nuclear pleomorphism and many tumour giant cells. The cerebral deposits showed the same histological picture as the primary tumour.

Discussion

The interest of this case history lies in the occurrence of three primary squamous-cell carcinomas in one patient over a period of 10 years. Our assumption that these three growths were, in fact, all primary growths must first be justified. It is often stated that Billroth postulated three criteria to establish the existence of multiple primary tumours: (1) they must be histologically distinct, (2) they must arise in different sites, and (3) they must each produce separate metastases. We were unable to trace the source of this statement, but in 1887 Billroth and Von Winiwarter wrote that primary carcinomas might arise in two quite different sites, and that their independence could be demonstrated with complete certainty when the two carcinomas showed different histological structures. They went on to say that sometimes each of the primary tumours spread to lymph nodes and that in the metastases the characteristic form of each primary tumour could be found. This cautious expression of opinion on the subject is quite different from the very strict criteria usually attributed to Billroth.

In this patient all the tumours were of the same basic cell type, but we consider that their independence can be justified by their different sites of origin, by their clinical behaviour, and on histological differences.

The cutaneous and vocal cord lesions were each histologically primary carcinomas, continuity between normal and invasive squamous epithelium being visible. In the tumour in the lung, continuity between normal and malignant epithelium was not demonstrable, but the microscopical appearances of the very poorly differentiated squamous carcinoma were characteristic of bronchogenic carcinoma. The central origin (Walter and Pryce, 1955) of the neoplastic mass also indicated a primary growth rather than a metastasis. The natural histories of the lesions support the histological findings because cutaneous and vocal cord epitheliomas rarely metastasize except to regional lymph nodes. The presence of cerebral metastases was likewise evidence that the lung lesion was a primary carcinoma.

The significance of the coincidence of these primary neoplasms must next be considered. All the lesions are in themselves common, and their fortuitous association in one patient is not impossible. The alternative explanation is that this patient was predisposed to malignant metaplasia of squamous epithelium. A review of the literature suggests that the last explanation is more likely to be the correct one.

Several authors have analysed series of patients with malignant neoplasms in an attempt to decide whether their incidence of multiple primaries was to be expected in a random distribution of cancer throughout the population. Warren and Gates (1932) and Bugher (1934), among others, concluded that multiple tumours occurred more often than would be expected. On the other hand, Peller (1941) thought that multiple cancer occurred less often than would be expected in a random distribution. The selection of cases, criteria for diagnosis, and methods of analysis varied widely in these reports, and this probably accounts for their differing conclusions.

Epstein and Shaw (1958) thought that a study of multiple neoplasms occurring in one particular system or tract would be more amenable to critical analysis than larger and more heterogeneous series. Out of 821 cases of primary carcinoma of the air and upper food passages they found 47 cases of multiple primary carcinoma; in 26 of these cases both primaries occurred in the air and upper food passages. The particular relationship between carcinoma of the bronchus and carcinoma of the larynx was emphasized by Cahan (1955), who studied 2,502 cases of carcinoma of the bronchus. Eighty-one of these patients suffered at one time from a neoplasm elsewhere in the body. This was in the larynx in 19 patients and the oral cavity in 18. From these reports it would appear that the frequency with which two neoplasms occur in the air and upper food passages is greater than would be expected in a chance distribution.

The probability that there was a systematic predisposition to carcinoma in this patient is increased by the sex incidence of the neoplasms, for all three are more common in males than in females. Intrinsic laryngeal carcinoma is over 13 times more common in males than in females (Curwen, Kennaway, and Kennaway, 1954), and squamous carcinoma of the skin is more than twice as common in males (Welton, Elliott, and Kimmelstiel, 1949). Carcinoma of the lung is five times more common in males (Registrar-General, 1955), and squamous-cell carcinoma of the bronchus has been reported to be 25 times more common in males (Moersch and McDonald, 1953).

The predisposition of large areas of tissue to neoplastic change is compatible with the theory of tumour formation put forward by Berenblum (1954). He views carcinogenesis as a long-drawn-out process consisting of two stages. Firstly, the tissue is initiated by the action of small amounts of specific carcinogen which converts a few normal cells into dormant tumour cells. The promotion of overt cancer in the initiated tissue is dependent on the exposure to non-specific factors, such as heat, light, or irritation, which would have no carcinogenic effects in tissue which had not been initiated. These views are supported by experimental evidence.

Discussing the environmental factors in the aetiology of cancer of the larynx, Wynder, Bross, and Day (1956) suggested that tobacco smoke might act as an initiating agent.

They also proposed that alcohol consumption acted as a promoter of carcinoma of the larynx.

It is reasonable to suppose that multiple primary tumours will occur with increasing frequency as the survival rate for cancer continues to improve with advances in diagnostic and therapeutic techniques. In this patient, for example, a complete cure of her skin and laryngeal carcinomas was effected by radiotherapy.

Summary

The case history is described of a woman who died at the age of 71 of a squamous-cell carcinoma of the bronchus after the successful treatment of two other squamous-cell carcinomas, on the face and on a vocal cord, in the last 10 years of her life.

From a review of the literature evidence is presented that suggests there was a systematic predisposition to cancer in this patient.

We acknowledge with thanks the interest and advice of Sir Daniel Davies. The patient had also been under the care of Miss G. Barry, Miss P. Wade, and Mr. J. D. McLaggan, and we are grateful to them for permission to publish this account.

REFERENCES

Berenblum, I. (1954). *Cancer Res.*, **14**, 471.
Billroth, C. A. T., and von Winiwarter, A. (1887). *Die allgemeine chirurgische Pathologie und Therapie*, 13th ed., p. 896. Reimer, Berlin.
Bugher, J. C. (1934). *Amer. J. Cancer*, **21**, 809.
Cahan, W. G. (1955). *Amer. J. Surg.*, **89**, 494.
Curwen, M. P., Kennaway, E. L., and Kennaway, N. M. (1954). *Brit. J. Cancer*, **8**, 181.
Epstein, S. S., and Shaw, H. J. (1953). *Cancer*, **11**, 326.
Moersch, H. J., and McDonald, J. R. (1953). *Dis. Chest*, **23**, 621.
Peller, S. (1941). *Amer. J. Hyg.*, Sect. A., **34**, 1.
Registrar-General (1955). *Statistical Review of England and Wales for the Year 1954: Part I, Tables, Medical*. H.M.S.O., London.
Walter, J. B., and Pryce, D. M. (1955). *Thorax*, **10**, 117.
Warren, S., and Gates, O. (1932). *Amer. J. Cancer*, **16**, 1358.
Welton, D. G., Elliott, J. A., and Kimmelstiel, P. (1949). *Arch. Derm. Syph. (Chicago)*, **60**, 277.
Wynder, E. L., Bross, I. J., and Day, E. (1956). *Cancer*, **9**, 86.

REPORT OF TWO CASES OF PRECOCIOUS PUBERTY

BY

JOSEPHINE DAVIDSON, M.B., M.R.C.O.G.

Obstetrician and Gynaecologist, Cumberland Infirmary, Carlisle

Precocious puberty is uncommon enough to warrant reporting. Various authors draw the line of precocity at different ages, but all are agreed that the onset of menstruation below the age of 8 is precocious, and in the two cases reported below menstruation began at the age of 5 and 2 respectively.

Precocity may be of cerebral, adrenal, or gonadal origin. Only where the origin is cerebral does true puberty occur—that is, development of secondary sex characters is accompanied by spermatogenesis or ovulation. Where the cause is adrenal or gonadal the testes or ovaries remain infantile and non-functioning.

Sex interest is uncommon in precocious children, but fertilization is possible in those of cerebral origin; for example, the case reported by Escomel (1939) of the Peruvian girl, Lina Medina, who first menstruated at 8 months, and at 5 years 8 months gave birth to a 6½-lb. (2,950-g.) boy.

Sexual precocity is usually associated with (1) greater physical activity—for example, the child walks early; (2) slight mental retardation with aggressiveness and bad temper—mental precocity is rare; (3) advanced skeletal development, giving an increase in height and weight, and an advance in the bone age with early closing of the epiphyses—therefore such children are tall in childhood, but short in adult life; (4) undisturbed dentition; and (5) a late menopause.

In "cerebral" precocity the stimulus, which may be functional or organic, is directly on the brain, and is associated with an increase in the pituitary gonadotrophins which stimulate spermatogenesis or ovulation. Where the cerebral precocity is functional or "constitutional," as described by Jolly (1955), the puberty is normal in every way, but occurs many years too early. The normal order of events is maintained—that is, breast development first, then pubic hair, menstruation, axillary hair, and often a white leucorrhoeal discharge some months before the first menstrual period. The cases here reported belong to this group, and it is the most common cause of precocious puberty in girls. Genetic factors may play a part, but there was no hereditary history in these cases. The organic causes of cerebral sexual precocity are due to stimulation of the posterior part of the hypothalamus by tumour, meningitis, or encephalitis, with an intact pituitary, as the eosinophil cells must be free to secrete an excess of gonadotrophins and so stimulate the gonads. Weinberger and Grant (1941) suggest that the lesion of the posterior hypothalamus removes the normal control or inhibitory force exerted over the pars distalis of the anterior lobe of the pituitary, which then releases excess gonadotrophins that stimulate the ovaries or testes to produce oestrin or androgen, which in turn produce the secondary sex characters.

Non-cerebral precocity may be due to (1) adrenal tumours or hyperplasia; these usually produce virilism; or (2) ovarian tumours, the commonest of which is the granulosa-cell tumour, which, however, is very rare in girls under 10. Where it occurs the bleedings are anovular and the other ovary remains infantile, as it is not stimulated by the pituitary, and there are no gonadotrophins present. The tumour is usually large and palpable by the time the genitalia and breasts are affected, and the urinary oestrogens are higher than the normal adult level of 40–600 I.U. Other rare ovarian tumours which occasionally produce precocity are teratomas and chorionepitheliomas.

The following cases fall into the group of functional or constitutional cerebral precocity, and their interest lies in the differential diagnosis and management. The management of such cases after diagnosis should be, in the words of Morse (1897), "complete abstinence of all therapeutic measures, but the psychological treatment is important." The mother should be given a full explanation, and warned of the possibility of pregnancy, and the girl should be encouraged to "think of herself not as different from others, but as capable of growing up faster than her friends" (Jolly, 1955).

Case 1

This child was born by spontaneous delivery at full term on October 3, 1947. Birth weight was 6.12 lb. (2,775 g.). She was breast-fed for four months, and first walked at 11 months. Breast development was first noted at age 3. Three elder sisters were normal in development. No genetic factor was present in the family.

She was first brought to the gynaecological clinic by her mother on July 13, 1953, at the age of 5¾ years, having had five days' vaginal bleeding two weeks previously. There was no pain and the child felt well. On examination she was an intelligent co-operative 5-year-old girl, tall for her age. The breast development was that of a 12-year-old

girl. There was no abdominal abnormality. The external genitalia were large for her age. A slight growth of pubic hair was present. It was decided to examine her under anaesthesia to exclude granulosa-cell tumour.

On examination under anaesthesia on August 4 the uterus was 2½ in. (5.7 cm.), and a shred of endometrium was obtained which showed microscopically a normal oestrin-phase picture. No ovarian tumour was palpable. *X*-ray examination of the skull showed no enlargement of the pituitary fossa, and the 17-ketosteroids were 3.9 mg. a day, which is high for her chronological age of 5 years but normal for her physiological age of 12+ years. Urine analysis in the middle of the cycle showed no free or combined oestrogens at the level of 8 I.U. a day, which excluded a granulosa-cell tumour of the ovary. An intravenous pyelogram showed normal kidney function with no displacement or caliceal abnormality on either side to suggest adrenal enlargement. The bleeding was therefore presumed to be due to functional or "constitutional" precocious puberty. She was seen at regular three-monthly intervals. The bleeding recurred at monthly intervals, regular from the first period; each lasted six days, was free from pain, and did not upset her. Her mother and school teacher were most co-operative, and the child seemed to suffer no psychological upset. The secondary sex characters showed steady development as time progressed, as did her height and weight.

FIG. 1.—Case 1. Patient aged 10 years. First menstruated at 5 years.

FIG. 2.—Case 1. Elbow-joint, showing all epiphyses fused. Therefore bone age of 18+ years, but chronological age 10 years.

We still see the child at six-monthly intervals, and the periods have continued to be of the type 6/28 days, and painless. The secondary sex characters have not greatly changed in the past year, and at the age of 10 (Fig. 1) she seemed perfectly normal mentally and well adjusted psychologically. She has menstruated regularly for four and a half years. Her skeletal age was 18 or more, with complete fusion of the head of the radius, capitellum, and medial epicondyle in the elbow, and the foot showed the metatarsal and phalangeal epiphyses fused (Figs. 2 and 3). Her height was 54 in. (137 cm.) (normal 52 in.; 132 cm.) and her weight 75 lb. (34 kg.) (normal 65 lb.; 29.5 kg.). Her urinary gonadotrophins were 10 mouse units a day and her total oestrogens 30 I.U. a day. These results are within normal limits for a female within the reproductive era, which is this girl's physiological state, but are high for her chronological age of 10.

Case 2

A girl was admitted to hospital on October 21, 1957, menstruating at the age of 3 years and 1 month. A clear history was difficult to obtain, as her mother was an Italian who spoke poor English and the father had left his wife a year previously. The child had been delivered by caesarean section for disproportion, and her birth weight was 8 lb. 3 oz. (3,715 g.). Walking occurred at 11 months. Breast development was noted at about 18 months, and slight pubic hair soon afterwards. She had slight vaginal bleeding at 22 months. The child was said to be quick and to have a good memory. She played well with her own age group. There was no family history of precocity, and the child had had no illnesses and had never complained of headache or abdominal pain. She was inordinately fond of sweets.

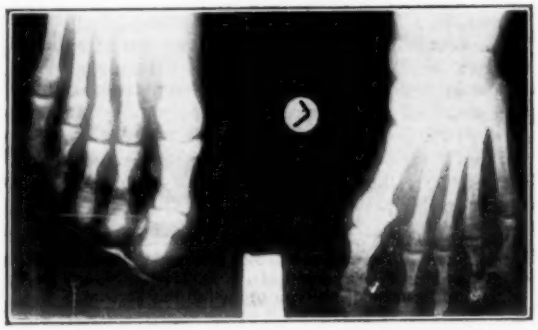


FIG. 3.—Left: Foot of normal child aged 10, showing metatarsal and phalangeal epiphyses. Right: Foot of Case 1, showing fusion of metatarsal and phalangeal epiphyses, and therefore a bone age of 18+.

On examination she was a pleasant little girl who gave the general appearance of a 6-year-old. Her height was 43 in. (109 cm.) (normal 36 in.; 91.5 cm.) and weight 53 lb. (24 kg.) (normal 32 lb.; 14 kg.). Her breast development (Fig. 4) was that of a 10–12-year-old, there was scanty pubic hair, and menstruation was fairly heavy. There was no palpable abdominal tumour.

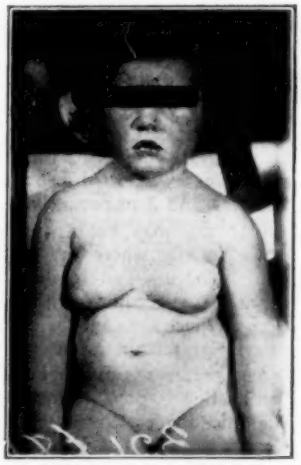


FIG. 4.—Case 2, aged 3.

On examination under anaesthesia on October 24 the uterus was 2½ in. (6.3 cm.) in length, and some scanty endometrium was obtained which showed normal endometrium with slight luteinization. The cervix dilated easily. There was no tumour of the ovaries palpable. Urine analysis showed a specific gravity of 1020; no glycosuria; no gonadotrophins at the level of 3 mouse units a day; total oestrogens 15 I.U. a day; 17-ketosteroids 2.3 mg. a day; and 17-ketogenic steroids 7.6 mg. a day. These bio-assays are consistent with a diagnosis of functional precocious puberty. A feminizing tumour of the ovary would give higher oestrin levels, and the 17-ketogenic steroids and 17-ketosteroids, though high for this girl's chronological age, were approximately normal for her physiological age of

12 years. *X*-ray examination of the elbow showed epiphysial development of a child of 10 years or over, with all epiphyses present and well formed (Fig. 5). The sella turcica was normal, with no erosion of the clinoid process.

FIG. 5.—Left: Radiograph of elbow (Case 2) at age 3, showing all epiphyses present and well formed—bone age therefore 10+ years. Right: Elbow of normal 3-year-old girl for comparison.

The mother was given a full explanation of the child's condition, and it was stressed that she must not be allowed to think of herself as being in any way abnormal, but just capable of growing up more quickly than other little girls of her age.

Summary

Two cases of constitutional cerebral precocious puberty are described, of girls aged 3 and 5 years. The clinical and biochemical investigations are described and emphasis is placed on the need for accurate diagnosis. In this group of precocious puberty there is no need for endocrine or surgical treatment, but there is a need for explanation and possible psychological treatment.

I thank Dr. W. G. Scott Harden, of the Cumberland Infirmary, for the *x*-ray films and Dr. J. Steven Faulds for photographs of them and of the children described, and also for his helpful advice. My thanks are also due to Dr. C. D. Paine and Dr. A. Jordan, of Sheffield, for undertaking the biochemical assays, and commenting on them.

REFERENCES

Escomel, E. (1939). *Presse méd.*, **47**, 875.
Jolly, H. (1955). *Sexual Precocity*. Blackwell, Oxford.
Morse, J. L. (1897). *Arch. Pediat.*, **14**, 241.
Weinberger, L. M., and Grant, F. C. (1941). *Arch. intern. Med.*, **67**, 762.

A note on the agricultural and horticultural use of lead arsenate, from the Ministry of Agriculture, Fisheries, and Food, states that this substance should present no hazard to consumers provided there is a minimum interval of six weeks between its last application to crops and harvesting. Nor should it be a hazard to operators provided they observe the following precautions: (1) *Dust and Paste Concentrates (Diluted and Used as a Spray).*—Wear rubber gloves when using the concentrate and avoid breathing the dust concentrate. Avoid contact with spray mist. Spray across wind when possible. Do not spray in high wind. If the eyes are contaminated with concentrate wash out immediately and thoroughly. If the skin is contaminated with concentrate wash immediately and thoroughly with soap and water. Wash exposed parts of the body before eating, drinking, smoking, and after spraying. (2) *Dust Concentrate (Used Undiluted as a Dusting Powder).*—Avoid breathing the dust. Wear rubber gloves and an efficient dust mask or other efficient protection for the nose and mouth when using the product. If the eyes or skin become contaminated treat as in (1) above, and again wash after spraying.

Medical Memoranda

Subacute Bacterial Endocarditis Treated with Oral Phenoxymethylpenicillin

While the successful treatment of a wide variety of infections with phenoxymethylpenicillin is now established (Hausmann and Zischinsky, 1953; Sinios, 1954), parenteral therapy is still preferred in such conditions as endocarditis, meningitis, syphilis, and peritonitis, until more data become available. It is therefore worth while reporting this case.

CASE REPORT

A girl of 15 who was known to have a congenital valvular lesion, recognized at the age of 1 year, was admitted to Stobhill General Hospital on May 1, 1956. She complained of malaise, fever, and cough with a mucoid sputum for three weeks; in addition, the sputum had been blood-stained for two days before admission. There was also a history of increasing dyspnoea on exertion.

In 1954 she had been a patient in Glasgow Western Infirmary with erythema nodosum, accompanied by pyrexia, tachycardia, and an increased erythrocyte sedimentation rate. She was assumed to have had a mild attack of rheumatic fever although there were no joint manifestations.

Examination and investigation established the diagnosis of aortic stenosis with subacute bacterial endocarditis due to a penicillin-sensitive strain of *Streptococcus viridans* which was cultured from the patient's blood on four occasions and was found to be highly sensitive to penicillin. The precise degree of sensitivity was not estimated.

Treatment with phenoxymethylpenicillin, 375 mg. (600,000 units) four-hourly, was begun on May 8. The temperature fell to normal on the 10th, but pyrexia recurred on the 21st. The dosage of penicillin was increased to 750 mg. (1,200,000) four-hourly, and the temperature settled on May 24 without recurrence. Treatment was terminated on June 30, a total of 280 mega units of phenoxymethylpenicillin having been given.

Clinical cure was indicated by sterile blood cultures, normal temperature, pulse, and E.S.R., which had all been elevated on admission, and by the disappearance of anaemia of normochromic type which had been present at the beginning of the antibiotic therapy.

The girl reported at the follow-up clinic on September 17, when she was noted to be keeping well and had begun office work. The haemoglobin and E.S.R. were normal and her weight was steady. On October 13 she was readmitted. There had been vomiting for one day and increasing dyspnoea during the previous two weeks. Her condition did not give rise to immediate alarm, but she suddenly collapsed and died about one hour after admission to the ward.

Necropsy.—The heart weighed 400 g. and the left ventricle was greatly hypertrophied. The aortic valve showed considerable distortion, the three cusps being greatly thickened and fused to form a membrane with a very narrow orifice. Numerous calcified nodules, due to healed subacute bacterial endocarditis, were present on the ventricular aspect of the valve cusps. On the mitral valve, along the cusp margins and chordae tendineae, there were slight nodular thickenings more suggestive of rheumatic endocarditis than of subacute bacterial type. Histological examination of the aortic cusps showed the nodules to be composed of fibrosis with patches of recent calcification: deep to the nodules and at their edges were areas of satisfactorily resolving inflammation with no evidence of recent exacerbation or of the presence of organisms. The cusps themselves and the bases of both mitral and aortic valves showed a scattered but denser fibrosis, consistent with valvular damage at the time of the earlier attack of rheumatic fever. The heart muscle also showed the patchy fibrosis of a previous rheumatic attack, but no Aschoff bodies or other recent lesions were found. No other organs showed naked-eye or histological abnormalities.

COMMENT

The treatment of subacute bacterial endocarditis with intramuscular preparations of penicillin is now well established (Cates and Christie, 1951; Finland, 1954), but involves frequent injections for a period lasting six to eight weeks.

The introduction of acid-stable phenoxymethylpenicillin is an advance in penicillin therapy, for adequate serum levels can be obtained with a dose of 200,000 units four-hourly (Martin *et al.*, 1956). In the treatment of subacute bacterial endocarditis, 1,000,000 units four-hourly has been recommended (Martin *et al.*, 1956), and this is supported by the dosage requirements of the present case. Finland (1954) has suggested that massive oral penicillin therapy might result in gastro-intestinal reactions similar to those seen after the administration of the broad-spectrum antibiotics. The cases reported by Quinn *et al.* (1956) as well as the present one did not develop any toxic manifestations related to the alimentary tract. Indeed, in the above case the patient tolerated the massive doses of penicillin without any undesirable effects whatsoever.

Histological study of the affected valve showed that the healing process was well established, although not yet completely resolved, as is to be expected with such dense lesions only two months after the cessation of treatment.

Conclusion.—In infections where the responsible organisms are not fully sensitive to penicillin, parenteral penicillin therapy is still to be preferred, in view of the high tissue levels that are required.

I am grateful to Dr. J. B. Rennie, under whose care this patient was treated, for permission to publish, and to Dr. J. C. Dick, consultant pathologist, for carrying out the post-mortem examination and for his advice regarding the findings.

GILMOUR HARRIS, M.B., F.R.F.P.S., M.R.C.P.,
Medical Registrar, Stobhill General Hospital, Glasgow.

REFERENCES

Cates, J. E., and Christie, R. V. (1951). *Quart. J. Med.*, **20**, 93.
Finland, M. (1954). *New Engl. J. Med.*, **250**, 372.
Hausmann, E., and Zischinsky, H. (1953). *Wien. med. Wschr.*, **103**, 725.
Martin, W. J., Nichols, D. R., and Heilman, F. R. (1956). *J. Amer. med. Ass.*, **160**, 928.
Quinn, E. L., Colville, J. M., Cox, F., and Truant, J. (1956). Ibid., **160**, 931.
Sinios, A. (1954). *Med. Klin.*, **49**, 2031.

Case of Cutis Verticis Gyrata in a Low-grade Microcephalic Spastic Male

The earliest case of cutis verticis gyrata reported in the literature appears to have been that of Robert (1843). The second and third recorded instances were observed by Auvert (1848), and subsequent cases were noted by Poggi (1884) and Lombroso (1890). McDowall (1893) and Cowan (1893) recorded the first occurrence of this abnormal scalp development in association with a microcephalic mental defective, and since that case report several other authors such as Möller (1903) and Jadassohn (1906) have described similar instances. In 1907 Unna presented three cases and coined the name cutis verticis gyrata. The latter is also known under additional terms, such as "corrugated skin," "bulldog scalp," and "pachydermie occipitale vorticillée."

The case presented here is that of a microcephalic quadriplegic male, functioning on a mentally severely defective level, who has been at the Caswell Training School, North Carolina, for about sixteen years. He is a white man aged 26 in whose paternal family history a case of insanity (grandmother) had been recorded. Otherwise no history of mental deficiency, epilepsy, or cutis verticis gyrata was noted.

He is a poorly nourished, completely helpless, spastic, quadriplegic, microcephalic idiot, without speech, and in appearance almost simian, with pronounced supraorbital ridges, low, narrow, receding forehead, and backward-bent neck (Fig. 1). There are some two dozen furrows in the scalp (Fig. 2), averaging 3 mm. in width and 3 to 5 mm. in depth, separated by folds that are about 1 to 1.5 cm. in width. The folds and furrows near the midline are more pronounced than those laterally placed, and they adhere to one another and are incapable of being obliterated by traction on the scalp. In addition to the antero-posterior folds

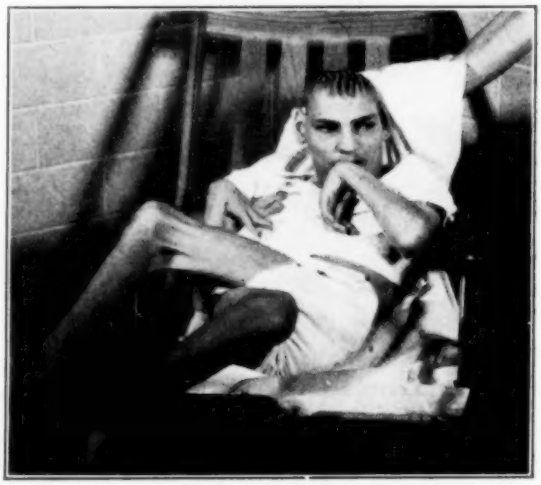


FIG. 1.—Photograph of patient.

and furrows, there are irregularities running transversely over the lower portions of the occipital and parietal parts of the head. Over the vertex these abnormalities are most conspicuous. The whole scalp acquires a corrugated cerebriform appearance, in which the folds and furrows of the scalp resemble the gyri and sulci of the brain surface. The hair is black and of fine texture.

FIG. 2.—Showing corrugated cerebriform appearance of scalp.

The cases cited in the literature were classified aetiologically by Polan and Butterworth (1953) as idiopathic or secondary types, the idiopathic type being ascribed to simple hypertrophy, to developmental anomaly, and to a reversion to a lower form of life; the secondary type being attributed to pathological conditions such as inflammatory changes, naevi, tumours, and various other miscellaneous diseases leading to the hypertrophy of the scalp tissues—for example, myxoedema, cretinism, leukaemia, acromegaly, syphilis, and tuberous sclerosis.

F. E. KRATTER, M.B., D.P.M.,
Lecturer on Mental Deficiency,
University of North Carolina, Chapel Hill, North Carolina.

REFERENCES

Auvert, A. (1848). *Clinica et Iconographia medico-chirurgica*, Paris, tab. VII. Abstract in Brun's *Handbuch der Praktischen Chirurgie*, 1854, Part 1, p. 91. Laupp, Tübingen.
Cowan, J. J. (1893). *J. ment. Sci.*, **39**, 539.
Jadassohn, J. (1906). *Verh. dtsch. derm. Ges.*, **9**, 451.
Lombroso, C. (1890). *Arch. Psichiat.*, **11**, 96.
McDowall, T. W. (1893). *J. ment. Sci.*, **39**, 62.
Möller, M. (1903). *Arch. Derm. Syph. (Berl.)*, **64**, 199.
Poggi (1884). *Arch. Psichiat.*, **5**, 323. (Translation in *J. ment. Sci.*, 1893, **39**, 226.)
Polan, S., and Butterworth, T. (1953). *Amer. J. ment. Defic.*, **57**, 613.
Robert, A. (1843). *J. Chir. Malgaigne*, **1**, 125.
Unna, P. G. (1907). *Mschr. prakt. Derm.*, **45**, 227.

Reviews

WHITBY AND BRITTON

Disorders of the Blood: Diagnosis, Pathology, Treatment, Technique. By Sir Lionel E. H. Whitby, C.V.O., *M.C.*, M.A., M.D.(Cantab.), F.R.C.P.(Lond.), D.P.H., and C. J. C. Britton, M.D.(New Zealand), D.P.H. Eighth edition. (Pp. 878+viii; illustrated. 75s.) London: J. and A. Churchill Ltd. 1957.

Our appreciation of this eighth edition of Whitby and Britton's textbook is clouded by the memory of the death of the senior author during its preparation. It reminds us how much solid scientific work Lionel Whitby completed, in addition to being a great man of affairs, and it makes lesser men admire the output of energy and the economy of effort which made all this possible. This textbook of 878 pages is an encyclopaedia of exact knowledge, carefully compiled and skilfully composed, and it represents an immense amount of study and the wise use of judgment. The main preoccupation of the reviewer of a book which was first published 23 years ago is whether it is retaining its freshness and not becoming a patchwork. This, happily, seems to be the case, and the authors have managed to incorporate a good deal of new knowledge with only a small increase in size. There is still probably more repetition than is necessary in discussing the anaemias of infancy, childhood, and pregnancy. The chapter on the biochemistry and cytochemistry of haemopoiesis will almost certainly have to be expanded, and the heterogeneous material in the chapter on disorders associated with splenomegaly could be better disposed elsewhere.

The main additions have been in the chapters on haemolytic diseases and haemorrhagic disorders. The greatest advance in haematology in recent years has been the recognition of the frequency of genetically determined abnormal haemoglobins as a cause of haemolytic anaemia, and the additive effect of abnormal haemoglobins in the individual who, for example, derives haemoglobin S from one parent and haemoglobin C from the other. The several varieties of haemoglobin have genetic, ethnological, and biological implications similar to those of the blood groups. A second advance in the haemolytic anaemias, less sweeping but still satisfactory, is the finding that the haemolytic anaemias produced by sulphonamides, primaquine, acetanilide, and favism are all due to an intrinsic defect in the red cell, apparently a deficiency in glutathione. This is more common in the negro, and therefore has attracted more attention in the U.S.A. In the haemorrhagic states much of the new work is of interest to the specialist only, but the recognition of the acute defibrination syndrome in pregnancy and its treatment by fibrinogen have an immediate clinical application. This textbook is a credit to British medicine, and British haematologists will join in wishing Dr. Britton every success in sustaining it at the same level in the future.

L. J. WITTS.

SKELETAL ANATOMY

Frazer's Anatomy of the Human Skeleton. Fifth edition, edited by A. S. Breathnach, M.D., M.Sc. (Pp. 247+viii; illustrated. 50s.) London: J. and A. Churchill, Ltd. 1958.

A basis of anatomy is essential to the teaching of all medical disciplines, but the amount and character of anatomy taught, and the books utilized as adjuncts to the teaching, clearly differ in undergraduate and postgraduate study. The undergraduate requires a dissecting manual and reference books to procure factual knowledge, but the postgraduate must utilize larger textbooks to augment his clinical knowledge of anatomy to the level necessary for examination purposes. The late Professor Frazer's *Anatomy of the Human Skeleton* has long been employed by postgraduates and teachers alike to extend their anatomical perspective in novel fashion. A new edition of the book is therefore welcome, although its format remains essentially unchanged, including the occasional omission of the definite article; most of the 197 illustrations consist of the now famous drawings of bones upon which all other anatomy is built, so well known in earlier editions. No attempt has been made to reduce markedly the amount of anatomical detail, but Dr. Breathnach in editing this new edition of the book has modernized the style and content in many places. Radiographs have been introduced for the first time, and the sections on the pelvis, arches of the foot, the skull, and craniometry have been almost entirely rewritten. The first chapter of the book has been very considerably revised, although the conception of the blood supply of bone now detailed may not exactly conform to modern ideas. Many other minor alterations have been made, but there is evidence of unnecessary adherence to antique terminology; thus the lateral occipito-odontoid ligaments (p. 24) have earlier (p. 20) already been described as the alar ligaments; and the term "multifidus spinae," for example, has now virtually disappeared from anatomical terminology.

This book retains its place as the authoritative contemporary textbook on osteology. It can be confidently recommended as an aid to postgraduate study, through which a wide knowledge of anatomy may be gained. It has stimulated many anatomists and surgeons in the past in their comprehension of topographical anatomy; the new edition should continue to do so with even greater facility.

R. G. HARRISON.

EXTRASENSORY PERCEPTION AND PSYCHOKINESIS

Parapsychology: Frontier Science of the Mind. A Survey of the Field, the Methods, and the Facts of ESP and PK Research. By J. B. Rhine and J. G. Pratt. (Pp. 220+ix; illustrated. 37s. 6d.) Oxford: Blackwell Scientific Publications. 1958.

This book, as its subtitle indicates, is "a survey of the field, the methods, and the results of E.S.P. and P.K. research." There has been so much controversy about E.S.P. (extrasensory perception) and P.K. (psychokinesis, or the ability of the mind to affect material objects directly) that this authoritative statement by the director and the assistant director of the Parapsychology Laboratory of Duke University appears at a particularly suitable time. For 30 years Rhine and Pratt have worked as pioneers in this field, and few readers will not be impressed with their easy mastery of the tremendous research literature and their competence in dealing in a strictly scientific way with the claims made and the results achieved.

For anyone interested in the subject, and not too prejudiced to have a look at the facts, this is undoubtedly the book to read. Relatively short and written in an easy style, it nevertheless succeeds in compressing an enormous amount of material, including a statistical appendix. The treatment is factual throughout, and where the writers discuss the applications of their research to fields such as medicine, psychiatry, education, or religion they are cautious and do not indulge in the wild claims sometimes made by less responsible writers. It is against this background of clear and calm discussion of experimental results that the facts are allowed to speak for themselves, and it is difficult not to come to the conclusion that a case for the existence of E.S.P., and to a somewhat less extent of P.K., has been abundantly proved. Admittedly the phenomena are somewhat capricious, and at times difficult to discover, but this is often true of pioneering research in any subject. The history of the neutrino in physics is equally characterized by this feature of "now you see it, now you don't," as is that of E.S.P. and P.K.; yet no one would deny the existence of neutrinoes. Critics have often condemned parapsychology on grounds which had but scant relation to the facts; the existence of this book should make it more

difficult for such criticism to arise, and should induce a calmer and more factual attitude in protagonists on one side or the other.

H. J. EYSENCK.

DRUGS AND THE BRAIN

Chemotherapy and the Central Nervous System. By Henry McIlwain, Ph.D., D.Sc. (Pp. 328+viii; illustrated. 45s.) London: J. and A. Churchill, Ltd. 1957.

This is a well-produced book with excellent figures and structural formulae. It comes from the pen of one who has been working for a good many years on problems related to the brain, and it should therefore attract much attention among the crowd of workers who have recently decided to study psychopharmacology. Perhaps the most useful part of the book is that concerned with the action of substances in nervous and mental disorders, where similarities in the effects are shown to be parallel to similarities in structure as in amphetamine and tetrahydro-β-naphthylamine. A full discussion of the clinical effects of substances like these might have been given, but it may be that the author wisely decided not to attempt this. The book gains throughout from its historical treatment of the development of different drugs. It is evident that the author has read Bullock's *History of Bacteriology* and Miss Marquardt's life of Ehrlich, and has done so with advantage. The book may not appeal at first sight to the clinician, because of the amount of chemistry it contains, but those who wish to grasp their subject in its entirety may be encouraged by the thought that the chemistry of drugs acting on the brain is not yet very extensive, and that taking it in is not yet too formidable a task. The style of writing is good, but could be improved. The author likes the verb "condition"—as, for example, "the properties of the nervous system . . . were conditioning the outcome of therapy." What he means is that they were "determining" the outcome of therapy. He speaks too of the "current status of bromides." A protest against this use of the word "status" should be made; in the United States it is continually used when the writer's imagination fails.

J. H. BURN.

PAEDIATRICS

Modern Trends in Paediatrics. Second series. Edited by A. Holzel, M.D., D.C.H., and J. P. M. Tizard, M.A., B.M., M.R.C.P., D.C.H. Foreword by Wilfrid Gaisford, M.D., M.Sc., F.R.C.P. (Pp. 372+xxiii. 70s.) London: Butterworth and Co. (Publishers) Ltd. 1958.

It is seven years since the late Sir Leonard Parsons edited the first series of *Modern Trends in Paediatrics*, and for the second series now available the editors are Dr. A. Holzel and Dr. J. P. M. Tizard. Twenty-one contributors cover a wide range of subjects. There are four from the United States, and the late Dr. J. Reinhold had just gone from England across the Atlantic before he died. Dr. J. H. P. Jonxis, from Holland, writes on "Chromatography and Electrophoresis." Dr. L. M. Sedova, from Russia, gives a fascinating account of the work of a paediatrician in a provincial town in his country. The remainder of the chapters are by British authors. It is difficult to pick out special topics for mention without producing a catalogue. On general impressions the volume gives a fair and balanced account of where paediatrics has got to, with a section in most chapters which takes a look at the future. Each reader will look for what interests him. For the reviewer, trying to be unbiased, the chapter on genetics by Dr. C. O. Carter was especially informative, and that on child psychiatry by Dr. D. W. Winnicott particularly exasperating: this contributor, modestly perhaps, does not yet appreciate how much he has influenced general paediatric thought and work. N. Veall, writing on isotopes, presents much that will be new to most paediatricians. Dr. W. P. D. Logan, describing trends of mortality in childhood, reminds paediatricians of the tasks ahead. The editors' choice of subjects cannot have been easy, and they have certainly succeeded both in this and in matching subjects and authors. This is a worthy successor to the first volume and a good review of modern paediatric work. Professor W. Gaisford provides a graceful foreword.

ALAN MONCRIEFF.

PEN-PICTURES OF PAEDIATRICIANS

Pediatric Profiles. Edited by Borden S. Veeder. Reprinted from the *Journal of Pediatrics*, November, 1954–November, 1957. (Pp. 267; illustrated. No price.) St. Louis: The C. V. Mosby Company. 1957.

In 1953 the editorial board of the *Journal of Pediatrics* came to a far-seeing decision when they undertook to publish a series of profiles or pen-pictures of medical men who had made signal contributions to American paediatrics during the first half of the present century. It was agreed that no living paediatricians should be included; and soon after the venture had been started it was decided to add profiles of a few paediatricians from other countries, men whose work had influenced the progress of paediatrics in America. The complete series has now been published in one volume, under the editorship of Dr. Borden S. Veeder. Thirty profiles appear, each written by someone who knew his subject personally, and in many cases had worked with him. The result is a fascinating gallery of pen-pictures—not official obituary notices or full-scale biographies—depicting famous men in their heyday. This is "living history" at its best, and the prospective reader need have no fear that his appetite will be surfeited with a sugary catalogue of high qualities unrelieved by human weaknesses. Virtues abound, of course, and especially dedication and determination; but these men were human, and the little inconsistencies, sometimes the irritabilities, and the occasional jolts to personal pride and ambition have not been glossed over. The authors were chosen with skill, and their contributions reach a very high level of good writing and close personal observation. Readers in this country will be especially interested in the British contingent—Barlow, Thompson, Still, Poynton, Findlay, and Parsons; but the series should be read consecutively if one is to get a true historical picture of American paediatrics during the past fifty years or so. And to those also who do not profess a special interest in paediatrics this volume will bring much pleasure and inspiration.

NORMAN B. CAPON.

Dr. Nathan W. Shock first published his *Classified Bibliography of Gerontology and Geriatrics* in 1951. This covered books and articles on every aspect of the subject published between 1900 and 1948. Quarterly additions to this list were printed in the *Journal of Gerontology*, and these have now been cumulated in the first *Supplement* to the bibliography, taking it to 1955. The present volume, like the original, is world-wide in scope and arranged under broad subject headings. It contains nearly 16,000 entries, and has author and subject indexes as well as a list of the journals cited and their abbreviations. As with the previous volume, the production has been made possible by the Forest Park Foundation, Peoria, Illinois. It is published in this country by the Oxford University Press at £6.

Volume III of *Spot Diagnosis* brings together a further series of cases for diagnosis, published originally in *Medicine Illustrated* and its successor the *British Journal of Clinical Practice*. It is described as an illustrated aid to visual diagnosis, each case being presented in pictorial form, with the correct diagnosis overleaf. A new feature in this volume is a section in which the confirmed diagnosis and management of certain cases are discussed. The book (141 pages, 118 illustrations; 10s. 6d.) is published by Harvey and Blythe, London.

A new edition of the *Catalogue of Lewis's Medical, Scientific and Technical Lending Library*, revised to the end of 1956, has recently been published. This most useful reference book, listing about 28,000 titles, is obtainable from H. K. Lewis and Co. Ltd., 136, Gower Street, London, W.C.1, price 42s. (25s. to subscribers).

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY MAY 24 1958

FELONIOUS SUICIDE

Opinion in the medical profession has for many years been overwhelmingly against treating attempted suicide as a criminal offence. It found expression in the report of the B.M.A.'s Committee on Psychiatry and the Law in 1947[1] and has done so again in a new report by the Joint Committee of the B.M.A. and the Magistrates Association.[2] The Medical Women's Federation has affirmed the same view,[3] and many medical men and women have individually done so at different times. There is no reason to suppose that the medical profession is out of step with lay people on the issue or with coroners.[4] Forfeiture of property to the Crown as a penalty for the crime of suicide was abolished as long ago as 1870 by an Act which "did no more than give legal effect to the established practice"[5]—a practice that dated from at least a century before that. During the last three or four decades coroners' juries have shown a notable and probably increasing reluctance to bring in verdicts of suicide without the qualification "while the balance of his mind was disturbed." All this deserves some emphasis, because the Home Secretary, when asked in a Parliamentary Question[6] on February 6 if he would introduce legislation to amend the law, said he had no evidence that the alteration of the basic concept of suicide as a crime "would be universally acceptable to public opinion." It is in fact difficult to think of legislation which would arouse less opposition, while to postpone it is to leave England and Wales lagging behind virtually every other country in the world, including Scotland.

The treating of suicide as a crime goes far back into the byways of history, deriving from religious ordinances, fiscal measures to swell the Crown's finances, natural abhorrence for the taking of human life, and rationalization of guilty feelings among friends and relations of the deceased person. Since no legal penalties now attach to the act of suicide, the importance of its being a crime is mainly that the attempt to commit it is in consequence a crime: and here penalties are inflicted. Figures given in the report of the B.M.A. and the Magistrates Association show that in 1946–55 the police knew of 44,946 cases of attempted suicide. Of these, 5,794 (13%) were brought to trial; 5,447 were found guilty and 308 of them sentenced to imprisonment. The terms of imprisonment are usually up to six months, occasionally longer.

The attempt to justify criminal proceedings is usually founded on two premises—first, that they deter other people from attempting to commit suicide; secondly, that in some cases they provide the only way of giving care and protection to the person so that he shall not repeat the offence. A comparison of statistics between different countries is hampered by the fact that so few (India and some of the States in the U.S.A.) continue to treat suicide as a crime, but it may be worth noting that suicide is about 1½ times as frequent in England and Wales, where it is a crime, as in Scotland, where it is not, and the number of attempted suicides probably bears a similar relationship to the number of suicides in both countries.[7] The argument that prosecution is for the person's own welfare is not shared by psychiatrists who have had experience of these cases, and many would agree with Phyllis Epps[8] that it is "out of keeping with modern psychiatric facilities and treatment." Moreover, a common misconception is that the present law is supported by a respectable antiquity; it is in fact barely 100 years old and almost accidental in origin. A court decision in 1854 ruled the criminality of attempted suicide as "a self-evident truth, and it became firmly established by later decisions."[5] It is thus the result not of deliberate policy but of "a mechanical legal logic working from a premise developed by mediaeval judges for the purposes of enriching the royal treasury."[5]

To members of the medical profession an attempt at suicide sounds a call for help. Many of these patients are depressives, and "in every depressive illness, at every age, there is a risk of suicide."[9] A considerable number of others are aggressive or inadequate psychopaths.[10] E. Stengel[11 12] has shown that suicidal attempts often have what he calls an appeal character. The fact that in some cases the person has no real intention of killing himself has incidentally led to the curious position by which convictions for attempted suicide take place "where there is no legal foundation for them in the evidence, properly considered."[5] But, spurious in intention or genuine, the great majority of persons attempting suicide are in

[1] Report of the B.M.A. Committee on Psychiatry and the Law, *Brit. med. J. Supplement*, 1947, **1**, 103.
[2] See summary at p. 1233.
[3] *J. med. Wom. Fed.*, 1958, **40**, 47.
[4] Thurston, G., *Med.-leg. J. (Camb.)*, 1958, **25**, 152.
[5] Williams, Glanville, *The Sanctity of Life and the Criminal Law*, 1958, London.
[6] *Hansard*, February 6, 1958, col. 1333.
[7] Batchelor, I. R. C., *Proc. roy. Soc. Med.*, 1958, **50**, 301.
[8] Epps, P., *Lancet*, 1957, **2**, 182.
[9] *Brit. med. J.*, 1956, **2**, 813.
[10] Batchelor, I. R. C., ibid., 1954, **1**, 1342.
[11] Stengel, E., *Proc. roy. Soc. Med.*, 1952, **45**, 613.
[12] —— and Cook, N. G., *J. forensic Med.*, 1954, **1**, 252.

urgent need of medical care. Such compulsory powers as are required for the welfare of these unfortunate people and of society are better modelled on those devised to help the mentally ill than on the criminal law. In Scotland, when the attempt at suicide has some additional features such that it constitutes a breach of the peace or includes the incitement of someone else to commit suicide, then legal action may be taken. The report of the B.M.A. and the Magistrates Association believes that the procedure in Scotland is a proper one, and recommends that the law of England and Wales should be amended to conform with it. An opportunity to do this may arise when legislation is prepared to give effect to some of the recommendations of the Royal Commission on the Law Relating to Mental Illness and Mental Deficiency.

THE INDUCTION OF LABOUR

Four years ago we wrote that, with increasing safety of lower-segment caesarean section and with antibiotics for the prevention and treatment of sepsis, the induction of labour was becoming more common.[1] The extent of this can be seen from the figures given elsewhere in this *Journal* by Mr. I. Cope and Mr. M. G. Pearson: the induction rate at Hammersmith Hospital rose from 2.1% in 1951 to 7.5% in 1953 and to 14.6% in 1956. Indeed, there have been earlier reports from British hospitals in which the induction rate was over 18%.[2 3] Cope and Pearson concern themselves first with methods of initiating labour. They used surgical induction, preceded by the time-honoured ritual of castor oil, enema, and bath—three measures presumably intended to make for inner and outer cleanliness and to stimulate uterine action. There is something to be said for the enema, if only that it minimizes soiling during the second stage of labour. In some countries the hot bath has been replaced by a radiant heat cradle over the abdomen. But many now consider that the administration of castor oil as part of a "medical induction" is inefficient and an unnecessary infliction on the pregnant woman. In 1871 F. P. Smith[4] wrote of castor oil seeds that "the pulp is rubbed into the soles of parturient women to hasten the birth of the child or the expulsion of the placenta"; but it was probably B. P. Watson in 1920 who chiefly popularized its use when he included a dose of castor oil in his routine for induction.[5] Now, in 1958, G. C. Nabors[6] has concluded from a small controlled series of inductions that castor oil is without influence in initiating or advancing labour.

At Hammersmith the triad of medical measures was followed by amniotomy, in most cases puncture of the hindwaters being combined with rupture of the forewaters. If labour did not begin within 24 hours, antibiotics were given. Until mid-1955 caesarean section was performed if labour was not established within 48 hours, but for the last 18 months of the period under review the interval was allowed to extend to 72 hours, and during this period an attempt was made to bring on labour by continuous intravenous oxytocin. This may explain why the section rate after surgical induction fell from 18.2% in 1955 to 14.1% in 1956. G. W. Theobald and his colleagues[7] used oxytocin in "physiological amounts" in the 22% of their patients whose labour did not start within 24 hours of sweeping the membranes and rupturing the forewaters: the section rate in this series was 9%. While some prefer to postpone giving oxytocin until it is clear that labour will not follow soon after rupture of the membranes, others combine the hormonal with the surgical induction, and still others precede amniotomy by oxytocin drip, especially if the cervix is not "ripe." The oxytocin sensitivity test of W. C. W. Nixon and C. N. Smyth[8] may prove to be a useful guide to whether an oxytocin drip should precede, accompany, or follow artificial rupture of the membranes, or be omitted as unnecessary.

The sevenfold increase in induction rate over the period of 1951–6 at the Hammersmith Hospital did not increase the overall caesarean section rate, which remained at 5.4%. But the section rate in the women induced was 14.5%, with a consequent rise in morbidity rate. The total perinatal mortality did not fall as the percentage of inductions rose, but the foetal loss in the induced group fell sharply. As the authors themselves hint, this fall may have been due to the inclusion of increasing numbers of patients in the induced group whose labours would elsewhere have been allowed to terminate naturally in the expectation of safe delivery of the baby: and their good foetal results in the induced group may have failed to affect the overall perinatal mortality because deaths in this group were few in relation to the others.

[1] *Brit. med. J.*, 1954, **2**, 855.
[2] Tennent, R. A., and Black, M. D., ibid., 1954, **2**, 833.
[3] Parker, R. B., *J. Obstet. Gynaec. Brit. Emp.*, 1957, **64**, 94.
[4] Smith, F. P., 1871, quoted by Nabors, G. C., 1958.
[5] Watson, B. P., *Amer. J. Obstet. Gynec.*, 1920, **1**, 70.
[6] Nabors, G. C., ibid., 1958, **75**, 36.
[7] Theobald, G. W., *et al.*, *J. Obstet. Gynaec. Brit. Emp.*, 1956, **63**, 641.
[8] Nixon, W. C. W., and Smyth, C. N., ibid., 1957, **64**, 35.
[9] Bancroft-Livingston, G., and Neill, D. W., ibid., 1957, **64**, 498.
[10] —— and Fisher, O. D., ibid., 1958, **65**, 1.
[11] —— and Neill, D. W., ibid., 1958, **65**, 4.
[12] Macafee, C. H. G., and Bancroft-Livingston, G., ibid., 1958, **65**, 7.
[13] Turnbull, E. P. N., and Walker, J., ibid., 1956, **63**, 553.
[14] Bender, S., ibid., 1952, **59**, 510.
[15] Zondek, B., and Goldberg, S., ibid., 1957, **64**, 1.

The major indication for induction is boldly given by Cope and Pearson as "suspected placental insufficiency." Under this heading are grouped cases of raised blood pressure in pregnancy, of post-maturity, of slight bleeding earlier in gestation, and of twin pregnancy at term. On clinical and experimental grounds placental insufficiency seems to be the main threat to the foetus in the toxaemias of pregnancy; but some would hold that if, as at Hammersmith Hospital, 120/80 is generally accepted as the upper limit of normal blood pressure, many unnecessary inductions will be performed. As to post-maturity, the concept of foetal hypoxia as the dangerous concomitant of prolonged gestation has been widely discussed, but some recent researches in Belfast[9–12] do not support this theory. A pregnancy marked by bleeding before the 28th week is more likely to end prematurely in the last trimester,[13] but not necessarily because of deciduo-placental damage and consequent placental insufficiency; this indication for induction, therefore, may not be generally accepted. The birth weight of a twin is the chief factor governing its survival,[14] and, in the absence of toxaemia, routine induction at term is not necessarily the best policy, especially as there is often a considerable disparity in the birth weights of twins. The outstanding, and unfortunate, fact is that there is as yet no safe, generally applicable, and reasonably accurate method of assessing placental function. B. Zondek and S. Goldberg[15] proffer hopes that the titre of urinary oestriol may yet serve as a reliable guide, but further research is required in this direction. Meanwhile the obstetrician has still to rely on his clinical judgment in deciding afresh in each case whether induction of labour will be of benefit to the baby's health or not.

MAINTAINING IMMUNITY TO POLIOMYELITIS

The U.S.A. field trials of poliomyelitis vaccine in 1954[1] showed that a formalin-killed vaccine could protect against paralytic poliomyelitis. Further evidence from many countries including the United Kingdom has since confirmed the value of vaccination against this disease. In the U.S.A. in 1957 a protection rate of about 90% in children receiving three doses of vaccine[2] was achieved. So far so good, but fresh problems arise, and the one foremost to-day is to determine the most effective way of maintaining immunity. As a first step the more that is known about immunity in this disease the better.

The mechanism of immunity is not fully understood. Although resistance is closely associated with the presence of circulating antibody, precise information on whether any particular level of antibody is necessary for protection is lacking. It may be that individuals with low amounts of antibody will be protected, or even with no detectable antibody at all by virtue of what Salk calls the hyper-reactive mechanism coming into operation. However, until more is known about this problem the first objective would seem to be the maintenance of measurable antibody levels.

Some important communications on this problem have been made in the last three years. On the question of dosage G. C. Brown and D. C. Smith[3] have demonstrated a better antibody response in infants and young children with three doses of vaccine than with two or one. Following up this work Brown and Smith and their colleagues[4] measured the levels of antibody in three groups of children over a three-year period. In the first group 63 children were studied. They had received three primary doses of vaccine in 1954 and a booster dose one year later in 1955. Serum specimens collected at the time of primary immunization and in 1955 and 1957 were tested for antibodies. In 1957, two years after the booster dose, the mean titres showed a fourfold decrease in antibody, which in effect brought the antibody level back to what it was at the time of the primary response. In some cases the titre was unchanged over this two-year period. Thirteen children with no pre-existing antibody at the time of primary immunization also responded to the booster dose, and the resulting decline was of the same order. In the second series 18 children were studied who had received a less potent vaccine in 1954. The immediate primary response was poor by comparison, but the effect of a booster dose one year later (1955) was to raise the antibody titre to the same level as in the first group. Here again over a two-year period a three- to fourfold decrease in antibody was encountered, with comparable titres for types 1 and 2 antibody but with a greater loss for type 3. In the third series, consisting of infants and young children, the actual levels of antibody were very much lower, though the rate of decrease was similar. However, even apart from their age this group is not strictly comparable, for these children had received varying doses (one to three) from different batches of vaccine, and had received their booster dose six months after the primary dose. Similar studies have been carried out by

[1] The Francis Report. Evaluation of 1954 Field Trial Vaccine Evaluation Centre. University of Michigan, April 12, 1955.
[2] *Poliomyelitis Surveillance Report, No. 137*, 1958.
[3] Brown, G. C., and Smith, D. C., *J. Amer. med. Ass.*, 1956, **161**, 399.
[4] —— —— Prothro, W. B., and Rowe, R. E., ibid., 1958, **166**, 1960.
[5] Salk, J. E., ibid., 1958, **167**, 1.
[6] Report to the Medical Research Council, *Brit. med. J.*, 1957, **1**, 366
[7] —— ibid., 1957, **2**, 1207.
[8] Salk, J. E., *J. Amer. med. Ass.*, 1956, **162**, 1451.

J. E. Salk[5] at Pittsburg. In a recent publication he presents fresh data on the maintenance of immunity following immunization and describes two cases in which a similar pattern of antibody response was produced and maintained over a three-to-four-year period. One child had received three primary doses of vaccine two weeks apart and no booster. The other had had one primary dose and a booster seven months later. These findings in individual cases, together with other data, on the slow decline of antibody point to the importance of an adequate antigenic stimulus in the first instance. Results of similar studies carried out in Great Britain with a formalin-killed vaccine incorporating the Brunenders strain have been published in a series of reports to the Medical Research Council. The first study,[6] on 196 children, showed a satisfactory immune response to two doses of vaccine. Eight to eleven months later a considerable decline in antibody was found, in particular to types 1 and 3.[7] A third dose given at this time produced a typical booster response with titres equal to or greater than those often found after natural infection. In a further follow-up, reported at p. 1206 of the *Journal* this week, 21 children were studied 18 months after primary immunization (with two doses). The decline in antibody was more evident, but the response to a third dose was similar to that in the previous group. In all these cases the type-2 antibody response was invariably the highest. In both the British and American series a number of children were encountered who had clearly developed an inapparent infection at some stage after the second dose, thus providing further evidence that killed vaccines will not interfere with natural subclinical infection. A small number of these children given a third dose of British vaccine developed exceptionally high antibody concentrations.[7]

If antibody levels are to be maintained after immunization, and this seems a reasonable objective at present, then a third dose of vaccine will be required. Further doses may be necessary, but time alone will show the need for them. J. E. Salk[8] has recommended two primary doses four to six weeks apart followed by a third seven months later. It may be necessary to delay the third dose for one reason or another, and from the British results it seems to work quite well after 18 months, but it would be a mistake to lose sight of it altogether. All these findings are of immense value and reflect great credit on those who carry out the work and on the parents and children who have taken part. It is only by investigations of this sort that we shall get the final answer to immunization against poliomyelitis.

PULSELESS DISEASE

William Harvey[1] and William Hunter[2] each described a case of unilateral absence of the pulse due to aortic aneurysm. Other causes of unilateral absence of the pulses in the upper limb include trauma, vascular occlusion by thrombosis, atheroma, or arteritis, and congenital anomalies of the radial artery; neoplasms obstruct the great vessels only if the artery is directly invaded. Bilateral absence of the arterial pulses is exceedingly rare, even in cases of aneurysm.[3 4]

In 1908 M. Takayashu,[5] a Japanese ophthalmologist, described the case of a young Japanese woman with absent carotid pulses whose retinae manifested "strange anastomoses of the central vessels" in a wreath about the papillae, and who gradually lost her sight from cataracts. Takayashu's patient is thought to be the first recorded case of a syndrome now described as "pulseless disease," "aortic arch syndrome," or "reversed coarctation." Sixty-nine cases have been reported from Japan, and 34 from Europe and America, including several in recent years.[6–14] An outstanding feature of the disorder is its predilection for young females, who outnumber males by 10 to 1. The fundamental lesion is an occlusion of the great vessels, commonly the brachio-cephalic trunks, close to their origin from the aorta, with consequent ischaemia of the brain, eyes, and upper limbs.

Clinically, pulsation of the carotid and subclavian arteries and their branches is absent; the blood pressure cannot be recorded in the arm by sphygmomanometry; and the patient complains of intermittent claudication. Gangrene is rare. Obstruction of the carotids gives rise to syncopal attacks frequently associated with convulsions and sometimes followed by transient hemiparesis. It has been suggested that hypersensitivity of the carotid sinus is the cause of syncope,[8] but obstruction of the vertebral flow from hyperextension of the neck was apparently the mechanism in one of E. Skipper and F. J. Flint's cases.[6] Ischaemic changes in the eye include irregularity of the retinal arteries, with peripapillary anastomoses and microaneurysms, a visible circulation with clumping of blood, lens cataracts, iris atrophy, and glaucoma. A rich anastomotic circulation develops through the intercostal and internal mammary arteries similar to that in aortic coarctation but with reversal of flow. A continuous murmur may be audible over large collateral vessels, and in the neck over the main arteries, owing to post-stenotic dilatation. A high blood pressure

[1] Harvey, W., *De Motu Cordis*, 1931, translated by C. D. Leake, Illinois.
[2] Hunter, W., *Med. Obs. Enqu.*, 1757, **1**, 323.
[3] Boyd, L. J., *Amer. J. med. Sci.*, 1924, **168**, 654.
[4] Hare, H. A., and Holder, C. A., ibid., 1899, **118**, 399.
[5] Takayashu, M., *Acta ophthal. Jap.*, 1908, **12**, 554.
[6] Skipper, E., and Flint, F. J., *Brit. med. J.*, 1952, **2**, 9.
[7] Caccamise, W. C., and Whitman, J. F., *Amer. Heart J.*, 1952, **44**, 629.
[8] Ross, R. S., and McKusick, V. A., *A.M.A. Arch. intern. Med.*, 1953, **92**, 701.
[9] Ask-Upmark, E., *Acta med. scand.*, 1954, **149**, 161.
[10] De Bes, L. T., Lucas, J. G. S., and Barcons, F. B., *Brit. Heart J.*, 1955, **17**, 484.
[11] Lessof, M., *Guy's Hosp. Rep.*, 1958, **107**, 53.
[12] Mengis, C. L., Dubilier, W., and Barry, K. G., *Amer. Heart J.*, 1958, **55**, 435.
[13] Sokmen, C., ibid., 1958, **55**, 433.
[14] Segal, F., and Berezowski, A., ibid., 1958, **55**, 443.
[15] Wendkos, M. H., and Rossman, P. L., ibid., 1943, **26**, 623.
[16] Starling, E. H., *Brit. med. J.*, 1925, **2**, 1163.
[17] Fishback, H. R., Dutra, F. E., and MacCamy, E. T., *J. Lab. clin. Med.*, 1943, **28**, 1187.
[18] Williams, A. H., and Schroeder, H. A., *Circulation*, 1951, **4**, 706.

in the legs has been recorded in about half the cases, but in healthy persons with well-developed thighs readings are normally raised.[15] R. S. Ross and V. A. McKusick,[8] who quote convincing experimental evidence,[16-18] suggest that hypertension arises from progressive cerebral ischaemia. The disease is slowly progressive, and after a period of blindness death usually ensues from cerebral infarction.

The aetiology in some reported cases was undoubtedly syphilitic, but in the majority of the young females serological tests were negative. Unfortunately, post-mortem examination has been reported in only six of the non-syphilitic cases.[12] The pathological process, which was restricted to the large arteries close to their origin, consisted of thickening and hardening of the adventitia; there was disruption of the elastic lamellae of the media by collagenous connective tissue and infiltration by round cells, plasma cells, and giant cells; the intima was thickened by atheromatous plaques and the lumen occluded by organized thrombus. Biopsy of peripheral vessels showed simple narrowing due to diminished blood flow, but no sign of arteritis. For diagnostic purposes the site of obstruction of the brachiocephalic trunks at their origin can be confirmed by aortography, which is preferable to angiocardiography.[14]

The aetiology of this rare form of arteritis occurring in young women is obscure. Temporal arteritis affects elderly men, and neither polyarteritis nodosa nor systemic lupus erythematosus is restricted to large vessels. The L.E. (lupus erythematosus) cell has not been reported in pulseless disease, but the sedimentation rate is usually high. Occlusion of a common brachiocephalic trunk could theoretically account for the circulatory disturbance, but, while congenital variation was apparently a contributory factor in six of the reported syphilitic cases, it is rarely the cause of pulseless disease. Further elucidation is dependent on full investigation of patients in the early stage. Probably this is a freak disorder caused by non-specific arteritis at an unusual site.

For the established case reconstructive surgery may soon be feasible and safe in selected cases. Ross and McKusick[8] describe successful relief of distressing syncope by resection of the carotid sinus. In the early phase of the disease steroid and anticoagulant therapy is worth a trial. M. Lessof[11] was disappointed with the result, but considerable physiological and symptomatic improvement has been noted (unpublished) in a patient who was treated with prednisolone from the onset.

ROYAL SOCIETY CONVERSAZIONE

While the latest and largest sputnik made its first orbit over Great Britain, the Royal Society had a number of exhibits appropriate to the satellite age at its conversazione last week. The most portentous was probably a model of "Zeta," which gives promise of a new source of atomic energy in a decade or so, but to the medical man "interferon" seems to open up almost equally remarkable possibilities. An exhibit of it was set out by Drs. D. C. Burke and A. Isaacs. Interferon was isolated from influenza virus by Dr. Isaacs and colleagues at the National Institute for Medical Research. It is a protein, is easily prepared, and is a potent inhibitor *in vitro* of influenza and related virus. The discovery of this substance is related to the well-known fact that infection with one virus interferes with the growth of another. Experiments in man have not yet been carried out.

Sir George Pickering and Mr. W. F. Cook, of the Radcliffe Infirmary, Oxford, demonstrated a strikingly ingenious experiment. They found that magnetic oxide of iron perfused through the renal artery of experimental animals could be made to lodge in the glomeruli; the renal cortex was then sieved and passed over a magnet. By this means glomeruli could be separated from tubules and other tissue, and estimation of renin—which raises blood pressure—in the three fractions showed that it was associated with the glomeruli.

Many people endure no sterner rigours of sledging than are to be found in the environs of Andermatt, but hardier souls who travel in the polar regions need something more than *croissants* and coffee for breakfast. An exhibit illustrating their daily rations, as provided for Greenland and Antarctic expeditions, was put on by Drs. H. E. Lewis and J. P. Masterton, of the National Institute for Medical Research, and Mr. T. C. Gallant, of the Metal Box Company. The ration provides about 4,800 calories daily, is scientifically packaged, and is pleasant to eat, though naturally it can hardly be compared with that gourmet's delight—marmalade pudding in the Army's "compo" rations. Another polar exhibit, by Mr. H. S. Wolff, also of the National Institute, showed underwear knitted from plastic-covered copper wire. Attached to a battery, it warms up the body; attached to a thermometer, it measures the skin temperature.

Genetical exhibits were much in evidence. Rival displays of snails from Oxford and Cambridge showed that the struggle for existence is as sustained among geneticists as it is among wild organisms. Exhibits from Oxford and Liverpool showed how and why some succulent species of butterflies escape predation by birds through their resemblance to distasteful species. And Professor C. D. Darlington and colleagues, of Oxford, elucidated by means of models some of the intricate behaviour of chromosomes during cell division. Finally, an exhibit by Dr. W. E. Swinton, of the British Museum (Natural History), showed that much can be deduced about the brain and special senses of dinosaurs, which lived about 100 million years ago, from the fossil remains of their skulls. Apparently they had excellent senses of smell, hearing, and sight.

GROUPING PATIENTS

Various systems are in common use for the classification of a large group of people so that they can receive attention more easily. The Army, for instance, puts the tallest on the right and the shortest on the left, while toastmasters begin with the highest social rank and work down to mere gentlemen. Yet another approved method

adorns the pages of the telephone directory, which begins with A and ends with Z. Certainly a classification by initial letter of surname has the air of depending on a decision that is at once impartial and indisputable, and no doubt that accounts for its popularity in all walks of life. But, owing to the uneven distribution of initials, trouble starts as soon as the attempt is made to split the group up into subgroups. If a group of patients is to be seen in four equal subgroups at, say, hourly intervals, and they are to be asked to come in accordance with the initial letter of the surname, how should the subgroups be made up? Should the first be the A–F's (six letters), or the A–E's (five letters), or half the alphabet?

Help in solving this problem comes in a note published recently by P. G. Gray,[1] of the Government Social Survey. He analysed the distribution of initial letters in about 50,000 surnames obtained from samples of parliamentary electors on the 1957–8 electoral roll. The commonest initial letter in England is B (11.0%), in Wales J (11.4%), and in Scotland M (21.1%). No sample contained enough X's or Z's to count. After B came H and S (both 9.2%) in England, W (9.1%) in Wales, and S (8.5%) in Scotland. From Gray's figures it seems that a division of a group into four approximately equal subgroups on their surname initials would give as the first group A–D in England, and A–E in both Wales and Scotland, while the last group would be S–Z in England, R–Z in Wales, and Q–Z in Scotland. Luckily the common twofold grouping of A–L and M–Z does not differ excessively from a half-and-half division, giving, for the first half, 55.5% in England, 56.6% in Wales, and 49.9% in Scotland.

ASCORBIC ACID AND SURGERY

The body's needs for ascorbic acid are known to be increased during wound healing and infection, and it might be supposed that the stress of major surgery would act in a similar manner. Information on this point is scanty, and the recent report by J. H. Crandon and his colleagues[2] on ascorbic acid economy in surgical patients is therefore welcome. Since urinary levels of the vitamin show considerable variation, it is necessary to use blood for the estimations. Here the buffy-coat concentration, though small, is more reliable than the level in the plasma, which alters rapidly with fluctuations in intake. By the standard method of J. H. Roe and C. A. Kuether[3] the normal plasma ascorbic acid averages 0.7 mg. per 100 ml. and the buffy-coat level 15–30 mg. per 100 g. Deficiency is indicated by values below 0.2 mg. per 100 ml. and 8 mg. per 100 g. respectively. In 105 patients undergoing surgery there was an average post-operative fall of 17 and 20% in the two levels, the greatest drop occurring in those patients with the highest initial values. There was, however, no correlation between the degree of fall and the type of surgery. The striking thing about these figures is the relatively minor effect of surgery, and this, as Crandon and colleagues point out, may be due to post-operative haemodilution rather than to the effect of an acute stress. It seems unlikely that human patients utilize ascorbic acid during stress in the same way as the experimental animal.

Ascorbic acid plays a part in the metabolism of tyrosine, and scorbutic patients excrete large amounts of tyrosyl derivatives after a test dose of this substance.[4] In the present investigation it was found that the ability to metabolize tyrosine correlated well with blood levels of ascorbic acid. Less than 2 g. of tyrosyl derivatives were excreted in the urine of healthy subjects over a three-day period following the ingestion of 30 g. of L-tyrosine. When ascorbic-acid deficiency existed, the amounts excreted ranged between 2 and 5 g. Many patients who were regarded as deficient on the evidence of both tests underwent operation without incident, and a study of a selected group of 46 whose wounds later broke down showed deficient blood levels in only 19. This does not imply that surgery is safe in the face of a known deficiency, and extra ascorbic acid should be given to patients with a poor dietary history or severe infection, and to those with complicating sepsis or delayed wound healing after surgery. It is probable that at least 200 mg. daily is necessary, and in some cases even greater amounts may be required. Moreover, other complications of operation may be attributable to ascorbic-acid deficiency, and there is a need for further research into this problem.

JUNIOR MEMBERS' FORUM

This year a new part is being added to the B.M.A.'s democratic machinery. Younger members are to have their own annual forum, to be known as the Junior Members' Forum, and the first is being held at B.M.A. House on June 14. As its name implies, it is intended as an open meeting in which junior members may discuss their particular problems. Any junior member may attend, but voting powers will be limited to those who have been appointed or elected to represent their colleagues in the different fields of practice—in this case hospital and general practice, the public health service, the Armed Forces, and medical teaching. The British Medical Students' Association will also be represented. Representatives appointed by the Junior Hospital Medical Staffs Group Committee, the Assistants and Young Practitioners Subcommittee, and the Medical Students and Newly Qualified Practitioners Subcommittee—that is to say, those Association committees which already serve the young doctors' interests—will be responsible for putting recommendations from the forum to the appropriate standing committees, which will be the link between the forum and the Council itself. One of the matters which this new body will be discussing on June 14 is its own scope and objects, and presumably this will include consideration of such constitutional matters as its electoral role and the definition of the term "junior member." For the present this has been fairly widely interpreted to include all those who are not yet fully established in the branch of medicine in which they intend finally to practise.

[1] Gray, P. G., *Appl. Stat.*, 1958, **7**, 58.
[2] Crandon, J. H., Landau, B., Mikal, S., Balmanno, J., Jefferson, M., and Mahoney, N., *New Engl. J. Med.*, 1958, **258**, 105.
[3] Roe, J. H., and Kuether, C. A., *J. biol. Chem.*, 1943, **147**, 399.
[4] Rogers, W. F., and Gardner, F. H., *J. Lab. clin. Med.*, 1949, **34**, 1491.

INTERNATIONAL SOCIETY OF INTERNAL MEDICINE

[FROM A SPECIAL CORRESPONDENT]

The Fifth Congress of the International Society of Internal Medicine (president, Sir RUSSELL BRAIN) was held in Philadelphia from April 23 to 26. It was attended by physicians from 43 countries. The items noted below are those thought most likely to interest British doctors. Some of the contributions were of considerable importance.

Anticoagulant Therapy

The first panel discussion was devoted to a consideration of anticoagulant therapy. The members of the panel were Dr. Tage Astrup (Copenhagen), Dr. Stuart W. Cosgriff (New York), Dr. James A. Evans (Boston), Professor Robert Hunter (Dundee), Dr. John W. Keyes (Detroit), Dr. Koller (Zurich), Dr. Paul E. Lucomsky (Moscow), and Dr. Murray Weiner (New York). The chairman was Dr. Irving S. Wright (New York). Dr. WRIGHT began by asking each member of the panel in turn what he thought of the use of anticoagulants in so-called good-risk cases of cardiac infarction. One said that he reserved these drugs for the most serious cases, but all the others advocated anticoagulants for every case of cardiac infarction. One reason given for this was that even in mild cases thromboembolic complications were fairly common, especially venous thrombosis, and anticoagulant therapy would reduce their incidence; another was that an apparently good-risk case sometimes became a bad-risk case within 24 hours, and the delay in starting anticoagulants might be crucial. Several of the panel added that they treated impending infarction with anticoagulants.

In cerebral vascular disease long-term therapy was generally thought to be fairly encouraging, particularly if the underlying lesion was thrombosis of the carotid or basilar artery. Short-term treatment was not successful, and patients with a systolic pressure over 200 mm. Hg or a diastolic pressure over 110 mm. Hg were specially liable to haemorrhage. Dr. ASTRUP pointed out that fibrinolytic activity, though low in the brain, was very high in the meninges. This might explain the tendency for cerebral infarction to be complicated by subarachnoid haemorrhage.

With regard to the intensity of treatment, the panel advocated maintaining a prothrombin time of between 30 and 35 seconds in acute cases, and around 25 seconds (that is, about 2 to 2½ times normal) in long-term treatment. Dr. COSGRIFF recommended the use of oral vitamin K_1 whenever the prothrombin time exceeded 35 seconds. It was well known that bleeding sometimes occurred at times when the prothrombin index was not particularly low, and Dr. KOLLER said that this was probably because the current methods of estimating the prothrombin time did not measure the actual factor responsible for blood clotting. He found that a test which depended on the Stuart-Prower factor gave results more closely related to the onset of bleeding. In support of this claim, Dr. Koller said that with Quick's method the prothrombin time often fell to a low level 48 hours after the start of anticoagulant therapy, although bleeding was rare in the first week; the Stuart test did not give a low reading for five days.

Dr. KEYES said that, once anticoagulant treatment was started in chronic rheumatic heart disease or in atrial fibrillation, it was usually necessary to continue it indefinitely. In general, however, the greatest benefit was observed in the first two years. After two years there was no significant difference between cases receiving anticoagulants and those not receiving them. If anticoagulants were withdrawn abruptly, there was some evidence of a rebound phenomenon, shown by a greater liability to thrombosis.

The panel emphasized the importance of educating the newly qualified doctor in the use of these potent and potentially dangerous drugs. It was also recommended that patients on anticoagulants should carry a card mentioning this fact in case they came under the care of another doctor on account of haemorrhage, syncope, or some other emergency. Professor HUNTER advocated the development of out-patient anticoagulant clinics. Other points which emerged in the course of discussion were: There is at present no generally reliable *bedside* test of prothrombin time. The time of day at which the prothrombin time is estimated does not matter. If a patient continues to develop thromboses in spite of adequate anticoagulant therapy the presence of underlying carcinoma, especially of the pancreas, should be considered. Patients very rarely become resistant to anticoagulants, however long treatment is continued. Fluctuations in activity are usually due to variation in degree of absorption, which may be due to diarrhoea or rarely to hardening of the outer layer of the tablets.

E.C.G. of Cardiac Infarction, and Hypertension

Dr. ALEXANDER L. MYASNIKOV (Moscow) described an interesting experiment designed to throw light on the genesis of the electrocardiogram of acute myocardial infarction. The heart of a healthy frog or rabbit was exposed, and a piece of necrotic muscle applied to the ventricle. When the E.C.G. of the intact animal was recorded, it was found to show ST elevation typical of acute infarction. Dr. Myasnikov believed that this pattern was due to the migration of potassium from the necrotic tissue into the adjacent healthy muscle. In support of this view was the finding that during the experiment the potassium content of the necrotic tissue fell while that of the underlying heart muscle rose. Dr. Myasnikov also reported experiments showing the importance of increased work of the heart in the development of cardiac infarction. Thus cardiac infarction could be produced in rabbits without ligation of any of the coronary arteries by combining cholesterol feeding with either forced exercise on a treadmill or narrowing of the aorta to produce hypertension. Thus the importance of rest in the treatment of coronary disease was emphasized.

Dr. ROBERT W. WILKINS (Boston) reported that chlorothiazide had a useful hypotensive action in essential hypertension in addition to its diuretic effect. He advocated a relatively small dose—e.g., 375 mg. daily. Sodium restriction was unnecessary, but potassium supplements were essential, potassium depletion being the main danger of this method of treatment. Dr. Wilkins had observed several cases of arrhythmia, and there had also been five sudden deaths, in some of which the drug might have played a part.

Dr. DAVID S. SHORT (London) discussed the pathogenesis of pulmonary hypertension in the light of recent haemodynamic and pathological studies. Post-mortem pulmonary arteriography had shown that a high pulmonary vascular resistance was always associated with widespread organic narrowing of the peripheral arteries and arterioles. Although this narrowing was due in part to obstruction of the lumen by thrombosis or intimal proliferation, the small arteries also showed a diffuse reduction in calibre and indistensibility. Dr. Short suggested as a working hypothesis that pulmonary hypertension developed in three stages. In the first place, it was likely that in certain individuals arterial constriction developed in response to a moderate rise in pulmonary arterial pressure, as suggested by Dr. Paul Wood. This arterial constriction might then be followed by organic shortening of the circular muscle and elastic laminae. Finally, thrombosis and intimal proliferation blocked the lumen so that the hypertension became irreversible.

Dr. STIG RADNER (Lund, Sweden) described a new technique for recording pressures from the aorta, pulmonary artery, and left atrium by means of a needle introduced into the chest at the suprasternal notch. This technique had been employed successfully in over 250 patients with normal or diseased hearts, and when correctly performed was safe and painless.

Medical Aspects of Cancer

One session, sponsored and arranged by the American Cancer Society, was devoted to a consideration of the medical aspects of cancer, under the chairmanship of Dr. Lowell T. Coggeshall (Chicago).

Dr. E. CUYLER HAMMOND (New York) discussed trends in cancer mortality and cure rates. The increase in the crude cancer death rate was largely due to the fact that people were living longer. When age was taken into account it was found that the cancer death rate for females had declined by about 10% in the past 20 years. The decline had been greatest for cancer of the liver and uterus; cancer of the breast had not altered, and cancer of the ovary had risen. The cancer death rate for males had increased, mainly because of the rising incidence of lung cancer. Deaths from leukaemia had also increased strikingly in males, but the mortality from gastric, liver, and skin cancer had fallen. Dr. Hammond pointed to the improvement in outlook following treatment as one of the most encouraging facts about cancer to-day. A comprehensive study from Connecticut showed that the five-year survival rate for cancer at all sites in both sexes had improved from 25% in the period 1935–40 to 32% in 1947–51. Among females the survival rate had improved from 29% to 38%. The greatest advances had been seen in the results of treatment of cancer of the colon, rectum, uterus (body and cervix), and prostate.

The value of exfoliative cytology in the diagnosis of cancer in the digestive tract was emphasized in a paper by Drs. WALTER L. PALMER, H. F. RASKIN, and J. B. KIRSNER (Chicago). They had studied 151 patients with lesions of the oesophagus, 69 of whom were subsequently proved to have carcinoma. Sixty-six of these 69 cases were identified cytologically, while the cells obtained from two patients with oesophagitis were incorrectly diagnosed as malignant. They had examined 871 patients with gastric lesions, of whom 131 were subsequently proved to have carcinoma or lymphoma. Of these, 125 were correctly diagnosed preoperatively, and there were four false positives. They had also examined 183 patients with lesions of the colon, 38 being subsequently proved to have carcinoma. A cytological diagnosis was made in 36, and there were no false positives. In the oesophagus, stomach, and colon, therefore, 95% of carcinomas had been correctly diagnosed by exfoliative cytology, and false positives were fewer than 1%. Dr. Palmer and his colleagues pointed out that this technique was more accurate than radiology in the diagnosis of cancer in these sites, but they also emphasized that it was a laborious procedure, and one which was at present unsuitable for routine use. The same technique was applicable to the diagnosis of cancer of the pancreas and biliary tract, but so far it had proved possible to identify malignant cells in only 60% of cases.

Dr. JAMES E. ECKENHOFF (Philadelphia) discussed the management of pain in cancer. For intractable pain in carcinoma of the pancreas he recommended injection of the coeliac ganglion by the posterior approach, first with procaine, and, if this gave relief, then with 25 to 35 ml. of 6% aqueous phenol. In the last months of a painful disease inhalations of trichlorethylene from an ordinary inhaler had helped. In the closing days he supplemented narcotics with the intravenous injection of a very dilute solution of thiopentone.

Poliomyelitis

The National Foundation for Infantile Paralysis sponsored and arranged a symposium under the chairmanship of Dr. Norman H. Topping (Philadelphia). Dr. JONAS E. SALK (Pittsburg) posed the question: Will poliomyelitis be controlled by killed-virus vaccine? Although admitting that no final answer could yet be given, Dr. Salk thought the evidence so far available was encouraging. Raised antibody titres had been shown to be maintained for at least four years, though this might not prove to be true of all individuals. There was also evidence that, even if antibody levels fell to zero, immunity might persist. It seemed that the degree of immunity was not adequately reflected by the antibody level measured in the laboratory. It seemed too that patients who had been adequately vaccinated in the past had a rapid enough antibody response to infection to protect their central nervous system. Dr. Salk emphasized that booster doses were essential because many children failed to respond to the first and even the second vaccination. Intradermal vaccination was unsatisfactory because of the small quantity of vaccine which could be introduced.

Dr. H. M. GELFAND (New Orleans) reported on the natural occurrence of poliovirus infections of Louisiana households before and after vaccination. Between 1953 and 1957, 106 households, each with a newborn baby, were kept under observation. Blood and faecal samples were collected at fixed intervals, and also whenever any infection occurred. These studies showed that in Louisiana infection with polioviruses occurred very early in life. Only 28% of those infected developed symptoms, and none developed paralysis. In 1957, following vaccination, the incidence of poliovirus infection was much lower than in the previous years. Dr. Gelfand did not, however, believe that this was the result of vaccination, because there appeared to be no significant change in the susceptibility of vaccinated subjects, or in the course of alimentary infection once virus was introduced into the home. It appeared, therefore, that killed-virus vaccine did not influence poliovirus dissemination.

Dr. HILARY KOPROWSKI (Philadelphia) described observations on immunization with living attenuated vaccine. The evidence so far available suggested that a single vaccination conferred long-lasting immunity. In order to secure protection against the three types of poliomyelitis virus, three separate vaccinations must be performed with intervals between them of 20 to 30 days.

The subsequent discussion emphasized the fact that there is still considerable difference of opinion in the U.S.A. regarding the efficacy of killed-virus vaccine.

Arthritis and Rheumatism

The problems of arthritis and rheumatism were discussed by a panel consisting of Drs. Elmer C. Bartels (Boston), Richard H. Freyberg (New York), David A. Long (London), Nanna Svartz (Stockholm), and Edward Scull (Hartford, Conn.), under the chairmanship of Dr. Philip S. Hench (Rochester, Minn.).

On the subject of whether aspirin is as effective as cortisone the panel felt that no proper comparison was yet possible, because the mechanism by which either drug produces its beneficial effect was still unknown; the differences might well be qualitative rather than simply quantitative. For the same reason, there was no logical basis for deciding whether the drugs should be used together or separately. If their fundamental action is different it would be rational to use them together. With regard to the optimum dose of prednisone for long-term treatment of arthritis, Dr. HENCH recommended 10 mg. daily for men, 8 mg. for premenopausal women, and 6 mg. for post-menopausal women. Some members of the panel used doses 50% greater than these.

The panel considered that the danger of a flare-up of infection during treatment with steroids had been greatly exaggerated, probably because of the adverse effect noted in animals. It was inadvisable to stop prednisone because of infection or of perforated ulcer. It might in fact be necessary to increase the dose. Gold was still valuable, especially in early cases of rheumatoid arthritis. It was less troublesome than cortisone, though also less powerful, and it took between three and six months to become effective.

In the treatment of gout, Dr. BARTELS said that both colchicine and phenylbutazone were almost 100% successful. Acute attacks could usually be aborted by a single

intramuscular injection of corticotrophin gel in a dose of 100 mg. Sometimes it was best to use two drugs in combination.

In spite of the danger of inducing leukaemia, the panel were unanimous that radiotherapy was still the most valuable therapeutic weapon in rheumatoid (ankylosing) spondylitis. It was emphasized that the lowest effective dose should be used. Phenylbutazone often gave relief, and was worth a trial first.

Drs. ROGER BLACK, JOSEPH BUNIM, and ERNEST SIMON (Bethesda, Maryland) reported on the side-effects of prednisone and prednisolone in the prolonged treatment of rheumatoid arthritis. They had studied 59 patients. The commonest serious complication was peptic ulceration, which developed in 15 patients: 5 developed gastric ulcer, 9 duodenal ulcer, and 1 had ulcers at both sites. Some of these patients were receiving less than 10 mg. of prednisone a day. Nine patients developed fractures; the vertebrae were involved 7 times, the ribs twice, and the pelvis twice. Two patients died from fulminating infections, and in three other cases death may have been due to steroid therapy. A satisfactory result without any important complication was obtained in 32 of the 59 patients.

Dr. SVARTZ described work in progress on the haemagglutinating factor in rheumatoid arthritis. A substance capable of agglutinating sensitized erythrocytes can be demonstrated in the serum of about 85% of patients with rheumatoid arthritis. Agglutination is also produced by serum from approximately 50% of patients with lupus erythematosus and scleroderma, and less commonly in other conditions. Dr. Svartz and her co-workers have shown that the haemagglutinating factor in rheumatoid arthritis is precipitable in cold, and that the haemagglutinating substances found in other collagen diseases remain in the supernatant fluid. By ultracentrifugalization of the cold precipitate, it has been established that the rheumatoid factor is present in fractions containing macroglobulins. As a result of this work it is possible to foresee a specific test for rheumatoid arthritis and similar specific tests for other collagen diseases.

"Preleukaemia," Steatorrhoea, and Carcinomatous Myoneuropathy

Dr. JOHN S. RICHARDSON (London) spoke on the significance of the "preleukaemic state." He said that in the early stages of leukaemia the appearance of the marrow and peripheral blood might suggest aplastic anaemia (with or without myelofibrosis), pancytopenia, agranulocytosis, or even megaloblastic anaemia. He presented six case histories illustrating this preleukaemic phase. In three patients the interval between the initial presentation with hypoplastic anaemia and the appearance of frank leukaemia averaged three months; in the other three it was 15 months. The difficulty in diagnosis was increased by the late appearance or complete absence of enlargement of the lymph nodes, liver, and spleen.

Professor A. C. FRAZER (Birmingham) read a paper on the diagnosis and treatment of steatorrhoea. In children with gluten-induced steatorrhoea there were usually bowel symptoms, but cases of coeliac disease sometimes presented with anaemia or dwarfism. In adults with gluten-sensitivity abdominal symptoms were more often absent, and patients presented with defective growth, iron-deficiency anaemia, folic acid deficiency, or ulceration of the tongue or mouth. Gluten-induced steatorrhoea in both children and adults responded satisfactorily to a gluten-free diet, together with replacement of folic acid and correction of any electrolyte imbalance. To prove that a case of steatorrhoea was due to gluten-sensitivity wheat gluten should be reintroduced for a few days; if the diagnosis was correct the steatorrhoea would reappear. Tropical sprue was not due to gluten sensitivity. Treatment consisted in leaving the endemic area and taking folic acid. In refractory cases repeated antibacterial therapy might be necessary.

Sir RUSSELL BRAIN (London) delivered a special lecture on carcinomatous myoneuropathies. He described a series of over 40 patients in whom carcinoma was associated with a disorder of the nervous system or muscles unrelated to metastases. In about two-thirds of the cases the nervous system was affected, and in about one-third the muscles. In the neuropathic cases the most clear-cut syndrome was subacute cerebellar degeneration, and after that a sensory neuropathy. The myopathic picture was of muscular weakness with loss of tendon reflexes, but without evidence of involvement of the nervous system. Myasthenic symptoms might be a part of this clinical picture, and might respond to some extent to neostigmine and similar drugs.

Other contributions by British workers included papers on the relationship of the ABO blood groups and diseases of the gastro-intestinal tract by Drs. C. A. CLARKE and R. B. MCCONNELL (Liverpool), and on acute Ménière's disease by Dr. R. E. SMITH (Rugby).

ATTEMPTED SUICIDE

CHANGES IN ENGLISH LAW WANTED

A report by a Joint Committee of the British Medical Association and the Magistrates Association* advocates that the law of England and Wales be amended to provide that suicide, and, consequently, attempted suicide, should no longer be a criminal offence as such. This excludes cases of suicide pact and incitement to suicide. So far as possible no case of attempted suicide should be brought before any court except, for example, if there is a breach of the peace. This is the practice in Scotland.

The report says that magistrates' courts can impose imprisonment without option of a fine for up to six months, while at Quarter Sessions or Assizes heavier penalties can be inflicted. In a recent case sentence of two years' imprisonment was imposed (though reduced on appeal to two months). From 1946–55, 5,794 attempted suicides in England and Wales were brought to trial and 5,447 found guilty; 308 were imprisoned without option of a fine. The total number known to the police was 44,946. During 1952–6 the courts disposed as follows of persons convicted of attempted suicide:

Sentence or order	Number	Percentage of total
Imprisonment:		
Up to 1 month	31	1.1
Over 1 month and up to 3 months	76	2.6
Over 3 months and up to 6 months	84	2.9
Over 6 months	3	0.1
Probation order	1,842	63.0
Conditional or absolute discharge, bound over	819	28.0
Fine	21	0.7
Otherwise disposed of	46	1.6
Total	2,922	100

The Committee received information from a number of consultants in general and mental hospitals, who were practically all agreed that the person who has attempted suicide

*_Members for B.M.A.:_ Dr. Doris Odlum (Chairman) (Bournemouth), Dr. A. Barker (Whitstable), Dr. F. Bodman (Bristol), Dr. R. Forbes (London), Dr. T. P. Rees (London), Dr. H. C. Maurice Williams (Southampton). _Members for Magistrates Association:_ Lady Adrian (Cambridge), Mrs. G. M. F. Bishop (Leicester), Mr. Seymour Collins (London), Sir Leonard Costello (Uffculme, Devon), Mr. G. J. Morley Jacob (London), Mrs. I. M. H. MacAdam (Leeds).

Members of the medical profession may obtain the report free of charge on application to the Secretary of the B.M.A.

(_Continued on p. 1234_)

To-day's Drugs

Under this heading we hope to publish from time to time authoritative notes on a selection of new drugs.

Adcortyl (E. R. Squibb and Sons Ltd.).—Tablets of triamcinolone, 1 mg. or 4 mg. **Ledercort** (Lederle Laboratories Division, Cyanamid of Great Britain Ltd.).—Tablets of triamcinolone, 4 mg.

This substance, triamcinolone, is the 9-alpha-fluoro-16 alpha-hydroxy derivative of prednisolone. The advantages claimed for it are that it does not cause retention of sodium or water and that it is slightly more potent a glucocorticoid or "antirheumatic" agent than prednisone or prednisolone. There is some evidence that peptic ulceration, osteoporosis, and psychic disturbances may be less common than with its predecessors, but wider clinical experience is needed to confirm or negative these early impressions. In addition to the well-known so-called side-effects seen with cortisone and the delta compounds, triamcinolone is said on occasion to produce anorexia, an intense erythema of face and neck, headache, and lassitude.

Indications for its use are as for cortisone and its analogues—rheumatoid arthritis, bronchial asthma, nephrosis, certain skin conditions (in particular psoriasis), leukaemia, and others—but as it causes no sodium retention it is not indicated in adrenocortical-deficiency states. Because of its failure to cause retention of sodium or water it may prove particularly helpful to patients with conditions likely to benefit from cortisone who have also signs of congestive heart failure.

(*Continued from p. 1233*)

is a case for medical and social care, and that the intervention of the law is undesirable and unnecessary.

England and Wales, India, and some of the American States are the only countries where suicide or attempted suicide is regarded as an offence. In Scotland no police action is taken in most cases and no charge is ever brought on the ground that attempted suicide is in itself a crime. But when circumstances demand it, a charge of breach of the peace is taken. The action of the individual at the time of the incident is not an issue in such a charge but only the fact that the behaviour has been to the breach of the public peace and annoyance or alarm of the lieges. The Committee believes that the procedure in Scotland is a proper one and recommends that the necessary amendments should be made to the law in England and Wales to provide that those cases of attempted suicide which it is necessary to bring before a court should be dealt with summarily as a breach of the peace. The Committee also recommends that careful attention should be paid to the extension of facilities for psychiatric treatment as and when possible.

"To sum up, a person who attempts to commit suicide must undoubtedly be in a state of mental distress and unhappiness and therefore needs special sympathy and understanding. Public opinion has moved in this direction and it is desirable that the law should be amended in accordance with this more compassionate and merciful outlook."

Life Assurance

The Committee understands that, though the practice varies, it is usual for suicide to be excluded from the contract for the first year, after which it is in most cases not treated as a disqualification for payment of the policy moneys, provided the premium has been paid in the usual way. But, if a person who had attempted suicide tried to secure a new policy, it would then be a hazard which would have to be assessed in the same way as any other illness. Where there is a history of attempted suicide the chances of securing a new policy would be fairly remote.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Duodenal Ulcer

SIR,—I was interested to read in your issue of March 15 the articles by Mr. Harold Burge and his associates (pp. 613 and 615), and also the leading article (p. 631), on vagotomy in the treatment of duodenal ulcer. Mr. Burge and his associates are to be congratulated on this careful study, and also for the development of a practical method to determine the completeness of vagotomy at the time of operation.

Although greatly pleased by the leading article, I do not like your statement ". . . nothing precise is known either of the aetiology or of the pathogenesis of duodenal ulcer." This is hardly a fair statement to make at the present time when we can reproduce the lesion readily in experimental animals, and the alterations in gastric secretory physiology under which these experimental ulcers regularly appear are well known and their relative significance fairly accurately appraised. With your permission, I should like to summarize the evidence in favour of a concept that I have recently developed[1]—namely, that duodenal ulcers are usually due to hypersecretion of gastric juice of nervous origin and that gastric ulcers are usually due to a hypersecretion of gastric juice of humoral origin. I discount the significance of a local decrease in resistance on the part of the mucosa as playing any frequent role in ulcer disease.

Duodenal ulcer patients usually secrete from three to ten times as much gastric juice in the fasting empty stomach at night as do normal people. If a hypersecretion of this degree is produced in experimental animals, ulcers in the duodenum regularly develop. When the vagus nerves to the stomach in duodenal ulcer patients are completely divided, the fasting nocturnal hypersecretion is abolished, indicating that it is of nervous origin. The ulcers usually heal if the vagotomy is complete, and recurrence is rare if an adequate drainage operation has been done to prevent stasis of food in the antrum. This statement is based on an experience of 1,300 patients with duodenal ulcer treated by vagotomy and a drainage operation in this clinic.

The following lines of evidence suggest that gastric ulcers are usually due to a hypersecretion of gastric juice of humoral or hormonal origin brought about by prolonged liberation of gastrin from the antrum. Approximately 20% of gastric ulcer patients have had a previous duodenal ulcer producing pyloric stenosis. This stenosis produces stasis of food in the stomach with prolonged contact with the antrum mucosa and also increased gastric motility, both of which are potent factors in releasing gastrin into the blood stream. 80% of gastric ulcer patients display stasis of food in the stomach as a result of decreased gastric motility. This decreased motility may be due to decreased tonus in the vagus nerves, inasmuch as these patients also display a fasting nocturnal gastric secretion less in amount than that found in normal people. The fasting nocturnal gastric secretion seems to be almost entirely nervous in origin. Experimental evidence indicates that stasis of food in the stomach due to gastric atony can produce a hypersecretion of gastric juice of humoral origin.

In the surgical treatment of intractable peptic ulcers, surgeons have long been aware of the relatively high incidence of gastro-jejunal ulcer after low gastric resection for duodenal ulcer, but of its almost complete absence after low gastric resection for gastric ulcer. In the first instance, removal of the antrum does not eliminate the cause of the hypersecretion, which is of nervous origin, and for this reason stoma ulcers are produced. On the other hand, removal of the antrum in gastric ulcer patients who display a low fasting night secretion is rarely followed by stoma ulcer, since the cause of the hypersecretion has been removed. While

these concepts obviously require additional experimental and clinical evidence before we can be sure of their validity, there is much to support them at the present time.—I am, etc.,

Chicago. LESTER R. DRAGSTEDT.

REFERENCE

[1] Dragstedt, L. R., *Amer. J. Roentgenol.*, 1956, **75**, 219.

Oestrogens and Breast Cancer

SIR,—In the annotation on this subject in your issue of May 10 (p. 1115) the impression is given that there is general acceptance of a simple oestrogen-dependence of breast cancer. The view of a single dependence of breast cancer has been untenable for some time. The effects of oophorectomy, as with the natural menopause, do indeed reduce the total oestrogen as measured by excretion products, but the complex changes of the menopause, either artificial or natural, appear to be the important feature in the regression of the tumour. This complex involves a gross alteration in both adrenal and pituitary function.

Such an alteration is of great importance, as is borne out by the clinical efficacy of both adrenalectomy and hypophysectomy. Moreover, the success of adrenalectomy is not dependent on the level of oestrogens before operation, and regression can also occur even when oestrogen remains after adrenalectomy. This must imply that the removal of some other adrenal product is of at least equal value to the removal of some oestrogen.

Finally, regression of cancer will occur after hypophysectomy, even though no oestrogen is detectable by present-day means before operation. All these findings suggest strongly that simple dependence on a single hormone is improbable and that the tumour, if hormone-dependent, is probably dependent on a mixture of hormones, oestrogenic, progestational, and pituitary in nature. Interference in any or all of these factors may be necessary to influence the hormone-dependent tumour. It should be also remembered that oophorectomy only reduces and practically never abolishes oestrogen secretion, and that a considerable number of patients after adrenalectomy still excrete oestrogen in measurable quantity—a factor which emphasizes the importance of the other hormonal influences.

This clinical evidence falls in line with the present experimental evidence that breast growth in an animal after hypophysectomy cannot be produced by any single hormone administration and requires at least three factors—an oestrogen, a progestogen, and a pituitary hormone.—I am, etc.,

London, E.C.1. E. F. SCOWEN.

To-day's Drugs

SIR,—The *British Medical Journal* is to be congratulated on the new item in its columns entitled "To-day's Drugs," introduced in the issue of May 3 (p. 1061). In the annotation (p. 1055) introducing this feature it is stated that "we hope to publish at intervals authoritative short notes giving practical guidance on new drugs and on older drugs appearing in new forms," which in effect covers most of the recent proprietary preparations. It is to be hoped that the "intervals" will not be greater than a week and that this scheme will be retrospective as well as prospective. It is also to be hoped that the layout of the items should be on the lines previously suggested by me[1] for describing pharmaceutical products in the form of a standard reference card and should also include the price.

Is it too much to hope that the *B.M.J.* will start a service for doctors like that compiled by the *Pharmaceutical Journal* for chemists, but without the latter's well-known disadvantages?[2] If the items in "To-day's Drugs" were laid out as suggested above, 7 by 5 in. (17.8 by 12.7 cm.) cards could be reprinted of those items and incorporated into an index run on the lines suggested by Mr. G. Raine[3] and subsidized by the pharmaceutical industry through the Association of British Pharmaceutical Industry, the exact details of which would have to be worked out.

Finally I wish to record my grateful thanks to those pharmaceutical firms who are taking note of my previous suggestions.—I am, etc.,

London, W.12 JOHN D. W. WHITNEY.

REFERENCES

[1] *Brit. med. J. Suppl.*, 1957, **2**, 7.
[2] *Brit. med. J.*, 1956, **2**, 1431.
[3] *Brit. med. J. Suppl.*, 1957, **2**, 76.

Vesico-vaginal Fistula

SIR,—In your leading article (*Journal*, May 10, p. 1110) you have written: "There is reason to suppose that even now there are unfortunate women in the *remoter* (my italics) parts of this country who, day in and day out, tolerate a seepage of urine believing that their condition is incurable," and you hint that we should try to find these unfortunate women and try to help them. By all means let the gynaecologists, general practitioners, and others search diligently for these women so that they may have the best that we have to offer, but let us not delude ourselves into thinking that they are easily found or easily handled, or that their restoration to health will necessarily be simple. The restoration of continence in some cases can be as difficult as any other task in gynaecological practice.

Within the past 10 years or so I have "found" a few women with persistent fistulae, and there is every reason to suppose that there are many more, but it is not necessarily in the "remoter parts of this country" that they hide themselves; it is more likely to be in the big towns. I, too, believe that these women should be sought out, but this is a much more difficult matter than may generally be realized.

Previous attempts at closure, often on top of the trauma causing the fistula, may have been much more of an ordeal than was really necessary, and even the thought of further surgery just cannot be faced. (I have notes of one woman who, in the six months before she was referred to me, had eight anaesthetics and three operations.) A further complication is that the distress of the dribbling incontinence can quite change a woman's nature. More than once I have observed an allegedly "difficult" patient change almost beyond recognition once her suffering was relieved. Also, previous attempts at closure may have been "successful," but only for a week or so while post-operative oedema lasted. The patient's hopes were raised by her dryness to such a level that the subsequent return of incontinence was devastating, bringing her near suicide level. She may be unwilling to go through it all again. The surgeon in charge, too, may not have helped by being much too light-hearted about the lesion and far too optimistic about the prognosis.

The protective shell into which the woman retires is illustrated by one patient, now cured and very grateful, whom I suspected of still having her fistula when I scrutinized her old hospital records: she had to be tricked even to coming to see me by sending the ambulance to her door against her last-minute wishes. Even then I had to overcome 18 years of resistance (the time she had been incontinent) on both her part and that of her husband. When eventually she was admitted to hospital she nearly walked out again. As it so happened, the repair was simple and successful.

The vesico-vaginal fistula seldom kills its victim, but it probably makes her life more of a misery than any other single condition, and so we must do all we can for those with this most distressing and humiliating affliction.—I am, etc.,

Sheffield, 3. C. SCOTT RUSSELL.

Polio Vaccination

SIR,—I appreciate the leading article on poliomyelitis vaccine which appeared in the *Journal* of May 3 (p. 1053). Your reference to tuberculosis as a bigger problem in this country than poliomyelitis is more than apt.

I wonder if the figure of "75 injections a day" which you quote in the article is correct. Was not the figure "75" intended to apply to a session of two and a half hours? During such a session my medical officers have for some months been able to give easily more than 75 injections. To allow an average of more than two minutes for performing each injection must surely presuppose that there is no preliminary planning and "streamlining" of the necessary

preparations associated with immunization clinics. Precision in planning a session by a medical officer and health visitor is an essential element in ensuring that a high average number of children are immunized. In recent months more that 100 injections have frequently been given by my staff during one session where only schoolchildren attended. This number is less when mothers attend for immunization of their children under 5 years of age at infant welfare clinics.—I am, etc.,

Caernarvon, N. Wales. D. E. PARRY PRITCHARD.

Dirty Habits

SIR,—I couldn't agree more strongly with Dr. Jno. Crawford's letter (*Journal*, April 19, p. 943) in which he suggests the need for education on dirty habits amongst the general public. I should think the evidence for washing hands after using the toilet was as low as one in twenty or one in thirty, taking a cross-section of the general public. You cannot blame the teenagers if the parents don't show a good example, even though they are taught clean habits themselves at school. The use of a hand-basin is not encouraged by the builders of houses to-day, where we find the lavatory and hand-basin in separate rooms.

I am in favour of a Government drive for education on such matters, possibly on T.V. or radio, and also by those who have the supervision of a large number of people such as matrons over nurses.—I am, etc.,

Virginia Water, Surrey. VIOLA C. CAMERON.

SIR,—Further to the correspondence on "Dirty Habits," a year ago I drew the attention of a toilet paper manufacturer to the fact that his folded sheets were perforated in a number of places on each side of the fold—surely the most active part of the paper—with the result that the hand was actually bare. His reply was that this was absolutely necessary in their manufacture.—I am, etc.,

Sheffield. CHARLES LIPP.

SIR,—I read with interest the letter signed by an anonymous doctor (*Journal*, May 10, p. 1120). I assume he is not engaged in general practice; if he is, I would like to know his solution to the thermometer problem.

All general practitioners are well aware that their thermometers are potential bearers of infection, and all have their own solutions. Washing in water well below boiling point or wiping with a cloth or even fanning with the hat only lead to a sense of false security. In my practice it is our custom (*a*) whenever possible to use the patient's own thermometer, thereby confining the infection to the household; (*b*) to start the day with a waistcoat pocket full of thermometers which as they are used are transferred to the other side. When one returns to the surgery the dirty thermometers and their cases are transferred to a pool in antiseptic solution from which they are drawn again some days later, one hopes reasonably purified. It is likely that "Doctor's" medical attendant uses some similar technique.—I am, etc.,

Enfield, Middlesex. H. R. SHEPHERD.

Salt-hoarding Syndrome

SIR,—The article by Drs. R. J. S. Metz and W. Cooper of a case of the "salt-hoarding syndrome" in the *Journal* of February 22 (p. 435) is a welcome addition to those previously recorded in the literature. Whilst not shedding any further light on the pathogenesis of the condition, the article certainly reaffirms Selkurt's[1] injunction that, "in view of the multiplicity of factors concerned with water and electrolyte balance that may be disturbed under the above circumstances, attempts to draw discrete conclusions from clinical observations are extremely hazardous." The fact that their patient had been in a coma for three weeks in a country hospital before coming under their care and that there was apparently no record of fluid and electrolyte balance available at all for that period adds to the difficulties in elucidating this complex problem. Furthermore, the administration by the intravenous route of a fluid containing 0.9% sodium chloride to their patient who was frankly dehydrated and hynernatraemic on admission was not calculated to alleviate this biochemical disturbance, whilst the subsequent daily amount of salt-free fluid given in an amount of 500 ml. in excess of the daily urinary output could not compensate for the amount lost by insensible loss through the skin and the expired air. An additional 1,000 ml. of intake fluid would have been necessary.

That water intake is important in persons suffering from severe cranio-cerebral trauma was suggested by the work of Stevenson *et al.*,[2] which showed that, when bilateral lesions were produced in the ventromedian nuclei of the hypothalamus in rats, a chronic hypodipsia and hypernatraemia was observed when the water intake was dependent upon oral consumption. In man, too, Welt *et al.*[3] pointed out that the development of severe water deficit and hypernatraemia in the stuporous or comatose patient who has a neurologic disorder may be caused by his impaired ability to experience and express the sensation of thirst. Engstrom and Liebman,[4] in fact, believe that most of the reported cases are due to an impaired thirst mechanism, diabetes insipidus, or both.

More recently, Gordon and Goldner,[5] in two most carefully documented cases of severe craniocerebral trauma in which hypernatraemia, azotaemia, and acidosis developed, demonstrated a state of severe water-depletion in their patients as being the underlying factor in the resulting biochemical disturbances and stated that the hypernatraemia produced represented a normal response by the volume-regulating mechanisms of the organism. It would seem to make little difference, they stated, whether the initial fluid deficit was caused by impaired osmoregulation in the supraopticohypophyseal system, excessive urea diuresis from increased catabolism of stress or from high-protein feeding mixtures, or marked extrarenal water loss.

Drs. Metz and Cooper's contention that severe dehydration is not responsible for the hyperelectrolytaemia because their patient had a daily urinary output of between 1 and 2 litres of urine with a specific gravity of 1012–1018 is a fallacious deduction. When the concentration of electrolytes in the urine remained at extremely low levels throughout the course of their patient's illness, I would have thought that a specific gravity figure of 1018 represented a valiant effort by the renal tubule to concentrate the urine. Had there been no dehydration, the extremely low concentration of electrolytes in the urine would surely have resulted in a specific gravity very much lower than 1012. In any event, as Gordon and Goldner[5] rightly point out, whether or not renal water loss is excessive for any given patient's intake is impossible to evaluate without knowing the approximate respiratory and skin water losses. A rather low urinary specific gravity and/or "normal" urinary flow recorded for some of the reported cases of neurogenic hypernatraemia may not be proof of a "good state of hydration" if a patient is febrile, sweating, or hyperpnoeic, or if dehydration had developed before the initial studies. Under these circumstances a normal urine volume might indicate a diabetes-insipidus-like state or renal tubular damage. These authors stress the fact that the patient who has severe craniocerebral trauma should be watched closely for excessive extrarenal water loss through skin or lungs, and for renal water loss that may be excessive under the circumstances, and that an average daily fluid intake of 2 or 3 litres may easily be inadequate. They suggest that an increasing sodium or non-protein nitrogen concentration may be early evidence of a water deficit and may be corroborated by an increase in the plasma-protein concentration and haematocrit level.—I am, etc.,

Johannesburg, South Africa. I. FREED.

REFERENCES

1 Selkurt, E. E., *Physiol. Rev.*, 1954, **34**, 287.
2 Stevenson, J. A. F., Welt, L. G., and Orloff, J., *Amer. J. Physiol.*, 1950, **161**, 35.
3 Welt, L. G., Seldin, D. W., Nelson, W. P., German, W. J., and Peters, J. P., *Arch. intern. Med.*, 1952, **90**, 355.
4 Engstrom, W. W., and Liebman, A., *Amer. J. Med.*, 1953, **15**, 180.
5 Gordon, G. L., and Goldner, Fred, ibid., 1957, **23**, 543.

Chlorothiazide

SIR,—Your annotation on chlorothiazide (*Journal*, April 26, p. 990) mentions the enhancing effect of this preparation on hypotensive drugs. It adds that it might thus be of particular value in the management of hypertensive cardiac failure.

Chlorothiazide has no action *per se* on the blood pressure. Harington and Kincaid-Smith[1] mention that chlorothiazide delays excretion of mecamylamine from the kidneys, but Bayliss, Fleming, and Rees pointed out that the enhancing effect of chlorothiazide on mecamylamine could not be wholly attributed to delayed excretion of the drug. It certainly cannot be attributed to biochemical imbalance through sodium or potassium depletion because of the time factor—the enhancing effect is manifest after the first dose. A further point is that such an enhancing action is not clearly and consistently seen with a combination of chlorothiazide and pentolinium. As Bayliss and his colleagues have shown, a dose of chlorothiazide as small as 0.25 g. greatly increases the hypotensive effect of mecamylamine.

The object of this letter is to lay stress on this fact, as it would be very dangerous if practitioners were to substitute chlorothiazide in full dosage for mersalyl in cases of hypertensive heart disease who are receiving treatment with mecamylamine.—I am, etc.,

London, N.19. E. MONTUSCHI.

REFERENCES

1 Harington, M., and Kincaid-Smith, P., *Lancet*, 1958, **1**, 403.
2 Bayliss, R. I. S., Fleming, P. R., and Rees, J. R., ibid., 1958, **1**, 529.

SIR,—In your annotation on chlorothiazide (*Journal*, April 26, p. 990) the price of this new oral diuretic is incorrectly stated. To prevent any misunderstanding that may arise, the attention of prescribing doctors is drawn to the correct basic N.H.S. price, which is 1s. 10½d. for 2 g. and not 7s. 6d. as printed. On this basis the average patient with cardiac oedema can be maintained for an approximate cost of 3s. 9d. per week.—I am, etc.,

Merck Sharpe and Dohme Ltd., Hoddesdon, Hertfordshire. JOHN H. FINGERHUT, Deputy Managing Director.

Mental Illness and Childbirth

SIR,—Your annotation on the above subject (*Journal*, April 26, p. 902) is of considerable interest to psychiatrists and also to obstetric teams.

Some years ago I carried out a small piece of clinical research into psychoses associated with pregnancy, on patients admitted to St. Patrick's Hospital, Dublin, over a five-year period, and my findings, though not based on large numbers, would, I think, throw some light on the points you raise. In particular, I was surprised at the considerable role which stress seemed to play (domestic, financial, fear of labour, etc.), but in my series the most malignant form of stress appeared to be that arising from parental opposition to the marriage, and especially if this opposition resulted in an estrangement from the patient's mother, with consequent loss of the latter's interest and affection. In the light of these findings, I think it should be possible, in many cases, for obstetric teams intelligently to anticipate such an outcome, and to take all possible preventive measures where stress of any kind seems in evidence.

The preponderance of breakdowns in the puerperium as compared with the period of pregnancy can, I think, be explained. Stress of any kind associated with pregnancy will always have a psychological association with labour, and will as a result call forth heroic efforts to remain stable until at least that event has been accomplished. (Similar breakdowns are often seen to follow such events as the passing of an important examination, the recovery of a relative from a long illness, etc.) Also, of course, such a stress, by reason of its lowering of nervous potential, is always cumulative in its effect.

Schizophrenic breakdowns associated with pregnancy cannot, I fear, be so easily explained, but fortunately they do not form a big percentage of the whole. Such an issue might be kept in mind where an unusual degree of lack of co-operation is experienced, and most especially if such lack of co-operation seems irrational or is associated with bizarre ideas or anxieties.—I am, etc.,

Pinner, Middlesex. ROBERT THOMPSON.

Hormone Therapy for Atherosclerosis

SIR,—I read with interest your leading article (*Journal*, March 1, p. 509) on the above subject. It may be of interest to note that a group of Saskatchewan scientists have introduced an effective hypocholesterolaemic agent which seems to surpass other treatments so far developed.[1,2] When nicotinic acid is administered in adequate dosages to hypercholesterolaemic humans there is a marked and significant decline in their cholesterol levels. Our results suggest that the use of large doses of nicotinic acid may prove to be the most practical method reducing cholesterol level without dietary restrictions. Altschul and his colleagues have shown that in rabbits normal or artificially raised serum cholesterol levels can be lowered by large doses of nicotinic acid and the well-known experimental atherosclerosis inhibited.[3-5]—I am, etc.,

Saskatchewan, Canada. P. O. O'REILLY.

REFERENCES

1 O'Reilly, P. O., Demay, M., and Kotlowski, K., *A.M.A. Arch. int. Med.*, 1957, **100**, 797.
2 —— *Canad. med. Ass. J.*, 1958, **78**, 402.
3 Altschul, R., *Z. Kreisl.-Forsch.*, 1956, **45**, 573.
4 —— Hoffer, A., and Stephen, J. D., *Arch. Biochem.*, 1955, **54**, 558.
5 —— and Hoffer, A., *Circulation*, 1957, **16**, 499.

Medical War Crimes

SIR,—May I endorse most sincerely the letter on medical war crimes in your issue of May 10 (p. 1121) from Dr. M. H. Armstrong Davison? It is in no spirit of revenge or Shylockian desire to extract the last pound of flesh that one is horrified to know that the Federal German Government sees fit to reinstate a practitioner such as Herta Oberheuser. Or to learn that virtually nothing has been done for the surviving victims of "scientific experiments" at Ravensbruck, Dachau, and the rest of the Nazi concentration camps. To take no action is to condone these outrages of justice and does not serve the cause of international understanding and world peace.

The British Medical Association has an immense international reputation which it would do nothing but enhance if it made known its opposition to the present attitude of the medical authorities of Federal Germany. I feel sure the Representative Body would endorse overwhelmingly any such action by the Association.—I am, etc.,

Camborne, Cornwall. ERIC TOWNSEND.

Tattooing

SIR,—Mr. Norman Lake in his interesting article on tattooing (*Journal*, May 10, p. 1084) does not pretend to list all the uses of this art or custom, but he omits one which certainly ought to be put on record, if this has not already been done.

Towards the end of the first world war I was for a time medically in charge of the refugees in Palestine. Among them were a number of Armenians who share with the Jews the distinction of being the most gifted and also the most persecuted race on earth. I noticed that practically all their children, and also many adults, were tattooed on the space between the thumb and index finger of the right hand with the Armenian cross (a square cross with each arm crossed and often with a small cross in each corner). When I asked the reason I was told that their children were so often stolen by the Turks or left orphans after the frequent massacres that this mark was tattooed to remind them of

their race and their faith. The point of tattooing the cross in that position was that at that time no Moslem would admit the sign of the cross inside his house, and no slave or concubine would be of any use if he or she had his or her right thumb or hand chopped off; so the sign meant death or freedom.

It is to be hoped that there is no need for such practices to-day, though this week we are specially asked to remember the refugee problem. It is sad to have to add that practically all these Armenian refugees perished shortly after they were repatriated in a massacre that took place as soon as the French withdrew from Syria, but this pathetic and heroic use of tattooing surely deserves noble mention in the long and curious history of the practice of pigmenting the human skin.—I am, etc.,

Winsford, Cheshire. W. N. LEAK.

Bemegride and Barbiturate Overdosage

SIR,—We would like to comment on the article by Dr. T. J. Thomson on "Clinical Studies on the Action of Bemegride in Barbiturate Overdosage" (*Journal*, April 26, p. 976). Dr. Thomson finds that bemegride does not produce earlier awakening in patients who have received 0.5 g. of thiopentone. Dr. Thomson correctly describes the difficulty of making the necessary observations. A possible explanation of his negative results is that he used a fixed amount of 50 mg. of bemegride. Bentel *et al.*[1] injected the bemegride until they obtained a positive effect and found that dosage varied from 25–100 mg. Bentel's procedure is more rational, as it allows for individual variation.

Especially interesting are Dr. Thomson's results with amylobarbitone. He found that oral administration of 0.6–1 g. followed by 50–100 mg. of bemegride produced an awakening followed by dysarthria, diplopia, and ataxia. The patients then relapsed into a sleep lasting 16 hours. This is again at variance with our own work.[2,3] We have fed a mixture of amylobarbitone with 12.5% bemegride. The highest dose of amylobarbitone used was 1.75 g. Three hours after ingestion the patients could be awakened to eat a hearty meal. Eight hours later they were awake and out of bed, and few of them behaved as though they were "intoxicated." Perhaps the simultaneous administration of the two drugs results in a better antagonism than the giving of bemegride after the barbiturate.

Finally it should be stressed that the main uses of bemegride are twofold: (*a*) The treatment of deep barbiturate coma whereby the patient is returned to a "safe state"—i.e., the vital reflexes are operating satisfactorily and the patient is not a nursing problem. No attempt should be made to restore consciousness. For the correct successful use of bemegride see Mears.[4] (*b*) A provocative test for epilepsy, where the drug seems superior to metrazol.[5]—We are, etc.,

F. H. SHAW.
S. GERSHON.

Melbourne, Australia.

REFERENCES

1. Bentel, H., Barlow, M. B., and Ginsberg, H., *Med. Proc.*, 1956, **2**, 198.
2. Gershon, S., and Shaw, F. H., *Brit. med. J.*, 1957, **2**, 1509.
3. Trautner, E. M., Murray, T. W., and Noack, C. H., ibid., 1957, **2**, 1514.
4. Mears, G. W., ibid., 1958, **1**, 757.
5. Andermann, K., *Med. J. Aust.*, 1957, **2**, 355.

Delivery of the Placenta

SIR,—I feel sure that Dr. G. R. Usmar, whose letter (*Journal*, May 10, p. 1123) I much enjoyed, will be delighted to learn that a straw of folk-lore must have alighted in Lincolnshire some two thousand years ago, for do we not read in the *Aphorisms* of Hippocrates[1]: "To expel the afterbirth, apply something to cause sneezing and compress the nostrils and the mouth," and then the seer of Cos goes on to remind us that "theory is the flower and not the root of experience."—I am, etc.,

London, W.1. V. B. GREEN-ARMYTAGE.

REFERENCE

1. Hippocrates, *Aphorisms*, xlix (Loeb edition). London, 1931.

Cancer in Operation Wounds

SIR,—We were interested to read your recent annotation about the contamination of operation wounds by cancer cells (*Journal*, April 19, p. 940). While implantation of growth has been found to account for nearly half the recurrences at the suture line, and recurrence is stated to have been decreased by the use of mercury perchloride washouts during the operation,[1,2] a much more rational approach to the problem, which includes not only local recurrences, but recurrences elsewhere due to spread of migrating cells released by the operation through the venous and lymphatic systems, would seem to be by the use of a suitable systemic chemotherapeutic agent. This problem has been recognized by Hungarian workers in this field.[3,4] Their work indicates quite clearly that experiments on rats inoculated with Guérin carcinoma and treated with "degranol" (mannomustine) give grounds for hoping that similar favourable results may also be obtained clinically.

Degranol is now being used experimentally in Hungary as a pre- and post-operative routine treatment, particularly in gastric intestinal and rectal cancer, to minimize the risk of tumour cells being spread or implanted by the operation. Preliminary results are encouraging, and it is hoped shortly to publish the findings after a sufficient number of cases have been followed up.

H. YARROW,
Managing Director,
Leda Chemicals Ltd. (Pharmaceutical Division).

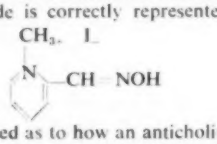
London, N.18.

REFERENCES

1. Goligher, J. C., Dukes, C. E., and Bussey, H. J. R., *Brit. J. Surg.*, 1951, **39**, 199.
2. Morgan, C. N., *J. roy. Coll. Surg. Edinb.*, 1955, **1**, 112.
3. Lapis, K., and Németh, L., *Brit. J. Cancer*, 1956, **10**, 719.
4. Selici, C., Németh, L., Eckhardt, S., and Kellner, B., *Mag. Tud. Akad. Biol. orv. Tud. Osztal. Közl.*, 1957, **8**, 119.

Action of P.A.M.

SIR,—I was interested to read your article on "Effective Therapy for Parathion Poisoning" (*Journal*, May 10, p. 1114). I would, however, point out that pyridine is a heterocyclic ring of an unsaturated nature, and 2-pyridine aldoxime methiodide is correctly represented thus:



I was also intrigued as to how an anticholinesterase caused a rise in blood pressure, the claim being that P.A.M. produces a fall in B.P. As anticholinesterases naturally potentiate vagal inhibition of the heart, I am surprised that these plant protection substances do not, in acute poisoning, cause profound slowing, with accompanying fall in blood pressure.—I am, etc.,

C. LAVENDER,
Pharmacy Student.

London, W.C.1.

Radical Cure of Malaria in Premunes

SIR,—The practitioner in malarious districts often experiences difficulty in determining if he has obtained radical cure of subtertian malaria in premunized patients who, upon returning home, are again exposed to infection. The resulting fresh attacks frequently are indistinguishable from recrudescence of their former infections. This situation is exemplified by the results of a course of treatment given to premune African schoolchildren, aged 6 to 12 years, living in a hyperendemic malarious district of Tanga Province, Tanganyika. Mosquito control measures or personal prophylaxis are not in use in the area. The children, infected asymptomatically with *Plasmodium falciparum*, received chloroquine diphosphate 0.225 g. base, with pyrimethamine 50 mg., on each of two consecutive days. Parasitaemia was cleared in all cases, but had returned in one-quarter of the children 5 weeks following treatment, and in somewhat more than half in 6 weeks. It was not known whether this return was from fresh infection only, implying success of the treatment, or from recrudescences, implying failure, or from both.

An opportunity to ascertain the curative value of this particular course of treatment has, however, been provided in another hyperendemic area of Tanganyika. In a small isolated settlement in Northern Province, named Mto wa Mbu (" Mosquito River "), all houses were sprayed with a long-acting residual insecticide in September, 1957, the work being carried out by staff of the Colonial Pesticides Research Unit, Arusha. Anopheline vectors had been decreasing in numbers through natural causes prior to the spraying, catches in June, 1957, producing 64.8 females per house, in July 11.8, and in August 0.9. Following spraying, the catches per house varied from 0.5 to 1.2 up to February, 1958, and sporozoites were absent from the few mosquitoes available for dissection.

On each of the two days, August 6 and 8, 1957, 92 African schoolchildren, aged 6 to 12 years, living in Mto wa Mbu and, for geographical reasons, unlikely to leave the settlement during the ensuing six months, received doses of chloroquine 0.225 g. base with pyrimethamine 50 mg. Their parasite rate at the beginning of treatment was 69, *P. falciparum* being found in 96% and *P. malariae* in 16% of the infections, many of which were mixed.

Seven weeks following treatment, and coincident with the residual spraying, 74 of the treated children were examined. One was infected, having subtertian parasitaemia in low density. Six months after treatment, 81 of the treated children were examined. Five were infected with subtertian parasites, and none with quartan. A contrast group of 41 classmates remained untreated in August, 1957. Six months later, 16 were found to be infected with subtertian or quartan parasites, or both.

It appears probable from these findings that recrudescence of the subtertian infections treated in August, 1957, did not occur, the few infections developing subsequently being attributable to a continuing low grade of transmission. In this event, radical cure was obtained in the premune children with 0.225 g. base chloroquine and 50 mg. pyrimethamine given on each of two days. Relapses of quartan malaria were not found 6 months after this treatment.

I am indebted to Dr. C. L. Hall, Senior Medical Officer, Northern Province, for personal administration of the drugs at Mto wa Mbu, and to the Director of Medical Services, Tanganyika, for permission to submit this note.

—I am, etc.,

Amani, Tanganyika. D. F. CLYDE.

Aphthous Ulcers

SIR,—I was interested to read the article on the treatment of aphthous ulceration in the mouth by Drs. S. C. Truelove and R. M. Morris-Owen (*Journal*, March 15, p. 603), as this is a frequent, painful, but relatively unstudied complaint. The authors did not describe the primary lesion preceding the ulcer. This is a vesicle full of yellowish serous fluid. I have several times seen such vesicles, although they are not often observed, as they are not painful and the patient does not notice them until they break, often as a result of being bitten. Their appearance is like some form of urticaria, and indeed suggests an allergic origin for the complaint. Not a few patients notice that they get these ulcers after eating walnuts, and a good number seem abnormally sensitive to unripe fruit.—I am, etc.,

Paris. ANDRÉ SCHLEMMER.

Value of Bronchoscopy

SIR,—I was very interested to read the article by Dr. A. R. Somner and his colleagues (*Journal*, May 10, p. 1079) concerning the value of bronchoscopy in clinical practice. I have had experience with just over 1,000 bronchoscopies in the last eight years and would like to stress the lack of morbidity after this investigation. In my series there was no fatality. Mild aspiration pneumonia developed in two cases; and in one there was a doubtful spread of a tuberculous lesion, but as a radiograph was not taken until one month after the bronchoscopy the connexion with this investigation was not certain.

In nearly 500 cases I have combined bronchoscopy with bronchography. The technique is simple. After bronchoscopic examination has been completed, the bronchoscope is withdrawn till the tip lies about half an inch (13 mm.) below the carina. The main bronchus thus exposed is sprayed with a surface anaesthetic through a Clerf's spray and the excess solution, if any, is removed by suction. The opaque medium is injected slowly through a Negus suction tube with gum elastic tip, the suction tube having been adapted to fit a bronchogram syringe. The bronchographic pictures were uniformly good and in many patients gave additional information. I consider that this method is especially valuable in cases of haemóptysis with clear radiographic pictures of the chest. In cases in which both bronchoscopy and bronchography are indicated it is a kindness to the patient to combine them.—I am, etc.,

Worcester. S. Z. KALINOWSKI.

Problems of Puberty

SIR,—The conflicting views on the subject of masturbation are even more clearly illustrated by Dr. Robert Thompson (*Journal*, May 3, p. 1064) than by previous correspondents. In my 30 years of practice I have never encountered any of those vaguely hinted " disastrous results " of masturbation that were not solely caused by the fear of such results implanted by well-meaning moralists in the adolescent.

During puberty the boy experiences for the first time the stimulating effect of the male hormone in force. With the production of semen the process of filling and emptying of the seminal vesicles takes its regulated course ; with the rising tension there are the inevitable erections, the equally inevitable sexual fantasies, and the relieving discharge of the waste product. This process does not end with adolescence, but continues throughout life. Whether the waste product leaves the body in a nocturnal emission, in urination, in intercourse, or in masturbation is, in my experience, without the slightest significance for the organic side of the personality. In the Middle East I found masturbation before marriage a generally accepted habit, regarded in the same light as the emptying of the bowels or of the urinary bladder. In fact, in many tribes of high moral standard it is considered to be an act of sexual hygiene by which the tension is lowered and the young man enabled to resist the temptation of defiling a woman of the tribe.

Those who have studied the phenomena of puberty in boys are familiar with that phase when every subject even vaguely connected with procreation is irresistibly attractive, when the slightest ambiguity leads to giggling, when the young mind is enticed by thoughts and topics normally considered taboo. That this adolescent fire receives fuel from the sexual aspect of literature, cinema, or advertisements is only to be expected. But these fantasies, while gratifying the need for immediate relief, do not satisfy the craving of the maturing boy for the reality of a flesh-and-blood love object, nor for his need for an exchange of affection. It is this process which leads to a normal maturation, and not any artificial suppression of a fantasy over which the boy has anyhow no control.

The association of masturbation with certain psychoses is no longer interpreted as the former causing the latter. Indeed, accessible patients have often explained to me that the sensation involved is the only pleasurable experience left when sleep, appetite, and all other external interests have vanished. It represents the last link between patient and the external world. That the welding of the sex urge with what Dr. Thompson calls " the tender emotions " is an ideal aim in marriage, nobody will deny, but this should not be attempted by means of instilling guilt-feelings in the young with dangerous untruths. Perhaps Dr. Ernest Jones was not so unreasonable when he stipulated that every psychiatrist should have undergone his own analysis before being let loose on humanity.—I am, etc.,

London, W.1. E. R. W. MONS.

SIR,—" Manners makyth man ": By manners, William of Wykeham meant morals or the manner of life. When the Chancellor founded his New College at Oxford in 1379 —this is what the motto of the College meant; the ten commandments and the laws of the Christian Church

were at that time recognized as the rules of life, and the single authority of the Church, in all matters concerning faith and morals, was paramount.

In England to-day every man who is not a Catholic appears to be his own Pope: recent letters to the *British Medical Journal* on sex matters show that each writer interprets the moral law according to his fancy. It is submitted that, apart from the confusion which such an attitude engenders, it is quite illogical. In the realm of government or even sport it would never be tolerated. (Imagine a golfer or a cricketer interpreting the rules to suit his fancy.) Ignorance of the rules is no excuse either on the golf course or in law. To pontificate to the extent that my interpretation is right gets one nowhere.

When, however, doctors (? in an endeavour to justify their own attitude) continue through the medium of the press to disaffect the young and uncritical and to say that abnormal behaviour in sexual matters is of no importance provided the subject has no sense of guilt, then surely it is time that the normal Englishman took notice and pointed out that the moral law cannot be changed to suit the whim or the weakness of the individual. Socrates must marvel that the poisoning of bodies is a matter for punishment but that poisoning of the mind is a matter for publication.—I am, etc.,

London, W.1. J. C. NEELY.

*** This correspondence is now closed.—ED., *B.M.J.*

Suicide as a Crime

SIR,—This subject interests me both as a doctor and as an anthropologist. Dr. Doris Odlum's reference (*Journal*, March 8, p. 579) to the point made by Professor Glanville Williams and Professor Mannheim in *The Times* of February 11 and 25 that only in India and some States of U.S.A. is attempted suicide regarded as a legal offence, and her observation that "in all other parts of the world, including Scotland, it is dealt with through the medical and social services, and they do not appear to feel the need for any legal sanctions," prompt me to make the following observations.

Let us take a look at what obtains in the neglected and so-called backward countries and we will see that this is a subject that has interested mankind all over the world for a long time. I am a member of the Ishan tribe in the Western Region of Nigeria. Before the advent of the white man in this area, a murderer robbed the king of a subject —a taxpayer; he, the murderer, not only forfeited his right to live but he and all he ever possessed, including the instrument used for the crime, automatically became the property of the Onojie (king). A man who had taken his own life, in Ishan custom, was a murderer of himself, and, appropriately, if the attempt to take his life failed he was tried for attempted murder.—I am, etc.,

Irrua, Nigeria. XTO G. OKOJIE.

Abuse of Legal Aid

SIR,—I was interested to read the article by your legal correspondent (*Journal*, April 26, p. 1009). One possible remedy, which I have pursued successfully, is for the defendant, or his solicitor, to make a representation to the Area Legal Aid Committee to revoke the plaintiff's certificate under Regulation 11 (2A) (b) of the Legal Aid (General) Regulations, 1950, on the ground that it is unreasonable in the particular circumstances for the plaintiff to continue to receive legal aid.

In my experience it is usually clear well before a case reaches court if a plaintiff is attempting to abuse the Legal Aid Scheme. In addition it may well be that it is to the defendant's solicitor rather than to the plaintiff's own solicitor that the abuse first becomes apparent, as a plaintiff who wishes to carry out some form of abuse will tend to withhold the true facts from everyone, including his own solicitor.—I am, etc.,

NIGEL RYLAND,
Legal Adviser,
Liverpool Regional Hospital Board.

Obituary

H. KIRKPATRICK, M.B., B.Ch., L.M.

Lieutenant-Colonel Henry Kirkpatrick, who had a distinguished career as an ophthalmologist in the Indian Medical Service and later in London, died peacefully at his home at Yateley, Hampshire, on May 11. He was 86 years of age.

A son of the Rev. George Kirkpatrick, of the Church of Ireland, Henry Kirkpatrick was born on October 28, 1871. He was educated at Marlborough College and Trinity College, Dublin, where he graduated M.B., B.Ch. in 1894. In that year he became house-surgeon at St. Mark's Eye and Ear Hospital and there studied ophthalmology under Story and Benson. He also had the advantages of clinical instruction from Swanzy and Werner, so that he became specially interested in eye work very early in his career. After several resident appointments he passed into the I.M.S. in 1898. Appointed physician on the staff of the General Hospital, Madras, after a period of military employment, he acted as professor of pathology in the university. In the latter post he was subsequently confirmed and he held both appointments for a number of years, during which he did much careful pathological work and established a high standard of teaching. For this purpose he reorganized the pathological museum, being ably assisted by the late Dr. Tirimurthi, who in time succeeded him. During these years also he often assisted Colonel R. H. Elliot, the superintendent of the Eye Hospital, and sometimes acted for him. In 1914, as a major, he succeeded Elliot as superintendent of the Government Ophthalmic Hospital and professor of ophthalmology. Promoted lieutenant-colonel in 1918, he left Madras in 1920 on leave pending retirement. In his six years at the Eye Hospital he supervised the construction of the Elliot School, a large teaching block, and greatly improved the facilities for postgraduate training, particularly in the field of pathology, in which he had such a long experience.

Kirkpatrick was a careful observer, an excellent surgeon, and a conscientious teacher. He made a great contribution to the advancement of ophthalmology in Southern India, and many of those who had the privilege of instruction at his hands, both in India and elsewhere, still value his guidance and will regret his passing. His kindly, placid nature, unfailing courtesy, and integrity earned for him affection and respect amongst all classes, Indian and European, patients and pupils. With such a superintendent, the only European on the staff, the atmosphere at the Government Ophthalmic Hospital among all ranks was a very happy one, and the team-work was excellent.

On retiring from Madras he started consulting practice in London in association with Elliot, and collaborated in the production of his textbook *Tropical Ophthalmology* (1920). He published two small volumes of his own, *Cataract and its Treatment* (1921) and *Diseases of the Eye* (1936), and made a number of other contributions to ophthalmic literature. He was ophthalmic surgeon to the Tropical Diseases Hospital and lecturer in ophthalmology at the London School of Hygiene and Tropical Medicine. A member of the Ophthalmological Society of the United Kingdom, he was also an honorary fellow of the American Academy of Ophthalmology. For a year, in 1922–3, he was a member of the Council of the B.M.A., and two years later he became chairman of the Willesden Division. In his leisure hours "Kirk" thoroughly enjoyed getting out into the country. A keen horseman, he loved hunting in his earlier days. Dry-fly fishing was always a source of joy, and work in his garden gave him great pleasure till near the end. In 1937 he relinquished his appointments in London, gave up consulting practice, and retired to Yateley.

In 1905 he married Edith Mary, daughter of Henry Eames, M.D., who survives him. To her and to their two daughters the sympathy of all who knew them will be extended.—R. E. W.

T. F. KENNEDY, O.B.E., M.B., B.Ch., D.P.H.

Brigadier T. F. Kennedy, principal medical officer of Remploy, Ltd., and formerly professor of hygiene at the Royal Army Medical College, died suddenly at Newcastle upon Tyne on April 25. He was 65 years of age.

Thomas Fuller Kennedy was born in Dublin on June 12, 1892, and was educated at Cork Grammar School and at University College, Cork. Graduating M.B., B.Ch., with first-class honours, from the National University of Ireland in 1914, he served in the R.A.M.C. during the first world war in Macedonia, Gallipoli, and the Balkans. He was appointed O.B.E. in 1919. A few years after taking the diploma in public health he became, in 1929, hygiene specialist with the Army School of Physical Training at Aldershot, with the rank of major. The work he carried out there investigating the energy expended during physical training exercises was the first attempt to grade scientifically the physical training tables for recruits of all arms. It was a most detailed piece of work, entailing long and intricate manipulations and the whole-hearted co-operation of the physical training staff, and it proved that the original empirical gradation of the exercises had been almost correct scientifically. The monograph he wrote as a result of this work was a model of conciseness and clarity.

Promoted lieutenant-colonel in April, 1939, he served during the second world war in the Middle East, returning to the United Kingdom to become professor of Army hygiene in the Royal Army Medical College, Millbank. In 1944 he became director of public health, civil affairs, 21 Army Group, and later principal medical officer of the Control Commission for Germany, when he was appointed a commander in the Netherlands Order of Orange of Nassau, with swords. It was almost a unique occasion when he returned to the Royal Army Medical College to become professor of hygiene for the second time. He retired in 1949 with the honorary rank of brigadier, and became principal medical officer of Remploy, Ltd., an appointment for which he was very well fitted. His outstanding characteristics were his kindness and his cheerfulness at all times. He was always friendly and ready to lend an ear and a helping hand to those who turned to him for advice or assistance. His great knowledge of his chosen subject was always at the disposal of junior officers, and his sudden death was a great shock to all those who knew him and appreciated his qualities.

Brigadier Kennedy married Miss Eileen Tebberer in 1925; she survives him, with one son and two daughters.

PHILIP GARSON, F.R.C.S.Ed., D.L.O.

Mr. Philip Garson, who was a consultant otorhinolaryngologist on the staff of the United Liverpool Hospitals, died in hospital on May 6. He was 57 years of age.

A son of the late Dr. W. R. J. Garson, an Orcadian who practised in Bebington, Birkenhead, Philip Garson was educated at Epsom College and at St. Bartholomew's Hospital, qualifying M.R.C.S., L.R.C.P. in 1924. As a postgraduate he obtained the Diploma in Laryngology and Otology of the English Royal Colleges in 1926 and the F.R.C.S.Ed. in 1928. After appointments at the Norfolk and Norwich Infirmary and at the Golden Square Ear, Nose, and Throat Hospital, London, Mr. Garson returned to Merseyside and became ear, nose, and throat consultant to several Liverpool hospitals. He will best be remembered for his work at the Liverpool Ear, Nose, and Throat Infirmary and the Northern Hospital, as well as at Clatterbridge and Hoylake cottage hospitals.

J. McG. writes: Mr. Philip Garson was an eminent and well-loved member of the medical profession. A man of a wide variety of interests and possessing a very keen intellect, he brought to his profession an abundance of kindness and sympathy which forbade mistrust of any of his fellow men. Those who had the privilege of meeting and working with him will testify to his unfailing interest and understanding of humanity. In spite of a series of illnesses over the past ten years, which he bore with typical courage and cheerfulness, he remained dedicated to the well-being of his patients, many of whom benefited from his exceptional surgical skill. Latterly his professional activities had been severely curtailed, and his death at the early age of 57 is a tragic loss to his colleagues and to the entire medical profession. He is survived by his devoted widow and four children, two of whom are married. His elder brother, Dr. Leslie Garson, practises in Bromborough, Cheshire.

Sir GEORGE WILSON, C.M.G., M.D., F.R.C.S.Ed. F.R.A.C.S., F.R.C.O.G., F.A.C.S.

Professor F. J. BROWNE writes from Wollstonecraft, Sydney, New South Wales:

The *Journal* of March 29 containing the obituary (p. 777) of Sir George Wilson, of Adelaide, reached me to-day (May 14). It was disappointing to find no reference to his pioneer work on antenatal care. He was, I believe, the first in the world to establish an outdoor antenatal clinic for the routine care of expectant mothers. His own description of the event, given to me in a private letter, is as follows: "I was in England in 1908–9, and, among other things, I saw what Ballantyne was doing in Edinburgh. When I returned to Australia I thought that all pregnant women should be examined during their pregnancy, and I obtained permission from the board of management of the Royal Adelaide Hospital to start a clinic for pregnant women. I held the clinic once a week, and, though the numbers were small, eight or ten each day, I carried on till I went away to the first world war in November, 1914. I had started the clinic in June, 1910." Two days later, on August 12, 1912, J. C. Windeyer, of Sydney, opened a similar clinic at the Royal Hospital for Women, Sydney. In May, 1911, a similar clinic had been opened at the Boston (U.S.A.) Lying-in Hospital. Wilson was a truly great man and fully deserved the honours conferred upon him in Britain and America.

CORYDON McA. WASSELL, M.D.

Dr. Corydon McA. Wassell, a medical hero of the second world war, died at his home at Little Rock, Arkansas, on May 12. He was 74 years of age. In an effort to save a group of wounded American sailors from falling into the hands of the enemy during the Japanese invasion of Java, he led the escape through jungle and over mountains. In spite of constant attack from the air he eventually succeeded in bringing 12 of the men safely to Australia.

Corydon McAlmont Wassell was born on July 4, 1884, and studied medicine at the University of Arkansas, graduating M.D. in 1909. After practising in his home State for some years he went out to China as a medical missionary. In 1927 he returned to the United States and became a health officer in Arkansas, making a special study of malaria control. He joined the U.S. Navy before the second world war, and was acting as a liaison officer in a Dutch hospital in Java before his epic march, for which he was awarded the Navy Cross and a personal citation from President Roosevelt. Promoted to rear-admiral, he remained in the Navy until 1947. He then returned, with his wife, to work in a medical mission on the Hawaiian island of Molokai. He finally retired to Little Rock.

Medico-Legal

CRIMINAL ABORTION AND MANSLAUGHTER

FIVE-YEAR SENTENCE ON DOCTOR

After a four-day trial at the Old Bailey, ending on Monday, Dr. L. A. Newton was convicted of criminal abortion and manslaughter. He was sentenced to five years' imprisonment. Dr. Ellis Stungo, who was charged with counselling Dr. Newton to procure the abortion, was dismissed from the case after the judge had found the prosecution's evidence against him insufficient to put to the jury. The trial was heard before Mr. Justice Ashworth.

Dr. Louis Aimee Newton, of Harley Street, was charged at the Central Criminal Court on May 14 with unlawfully using an instrument with intent to procure the miscarriage of Jean Josephine Florence Cook, aged 35, a single woman, on October 11 last year. Dr. Ellis Stungo, a psychiatrist, of Harley House, Marylebone Road, was charged with counselling and procuring Dr. Newton to commit that offence. Both pleaded not guilty. Dr. Newton also pleaded not guilty to unlawfully killing Miss Cook on October 24, 1957, and on a Coroner's Inquisition (*Journal*, March 29, p. 778) he further pleaded not guilty to the manslaughter of Miss Cook. Dr. Newton was defended by Mr. Gerald Howard, Q.C., and Dr. Stungo by Mr. Norman Richards, Q.C.

Case for the Prosecution

Mr. R. E. Seaton, prosecuting, said Miss Cook was an Australian nurse who came to Britain last July. She died on October 24, 1957, in the National Temperance Hospital, and the cause of death was an injection of utus paste which had been administered by Dr. Newton with intent to procure her miscarriage. Counsel said he understood it would not be disputed that the operation was performed. The jury would have to decide whether the operation carried out by Dr. Newton was performed in good faith in order to save the life of Miss Cook. In a case in 1939 which was similar in some respects to the one they were now trying, Mr. Justice Macnaughten had said, "And, if the doctor is of opinion that the probable consequence of the continuance of the pregnancy will be to make the woman a physical or mental wreck, the jury are entitled to take the view that the doctor who operates is operating for the purpose of preserving the life of the mother." If the jury came to the conclusion that had Miss Cook's pregnancy been allowed to continue she would have become a physical or mental wreck, then the defendants were entitled to be acquitted.

Both Dr. Newton and Dr. Stungo were fully qualified medical men. What was suggested was that Dr. Stungo was an accessory before the fact in that he passed Miss Cook on to Dr. Newton with the recommendation that her pregnancy should be terminated, and agreeing that it should be done.

There was a second charge against Dr. Newton, that he unlawfully killed Miss Cook, continued Counsel. If the jury came to the conclusion that this was an unlawful termination of pregnancy and that Miss Cook died as a result of the operation, then they should find Dr. Newton guilty of manslaughter. But supposing the jury came to the conclusion that they were not satisfied that the operation was unlawful, there was a second ground upon which, in the submission of the prosecution, they should find him guilty of manslaughter. The circumstances in which the operation was performed, and what Dr. Newton did after the operation, indicated, in the submission of the Crown, that he was grossly and criminally negligent in his treatment of the patient, thereby hastening her death. If the jury found that Dr. Newton was grossly and criminally negligent in his treatment, then they should still find him guilty of manslaughter.

Miss Cook's Medical History

After arriving in this country Miss Cook went to stay with a friend in Yorkshire, and whilst there she complained of sickness. The local doctor who saw her came to the conclusion that she was pregnant. Miss Cook came to London and saw a psychiatrist named Dr. Parsons. Dr. Parsons referred her to a Dr. Sugden with a letter stating she was depressed and obviously in a state of acute anxiety, and that she appeared unable to tolerate her pregnancy. Miss Cook saw Dr. Sugden, but he did not carry out any operation. A few days later Miss Cook moved to the Mapleton Hotel in Coventry Street, and on October 11 she was seen by Dr. Stungo. As a result of the interview with Dr. Stungo Miss Cook was passed on to Dr. Newton, and the same evening Dr. Newton performed an operation to terminate her pregnancy.

At the time of the injection Miss Cook apparently suffered intense pain. She returned to her hotel by herself, and became ill within a matter of twelve hours; by next morning she was vomiting. According to the chambermaid she looked yellow and drawn and was clearly a sick woman. All that day she remained in her room. Eventually Dr. Newton was summoned and he gave her some antibiotic pills, but they had no effect. The vomiting continued, and, what was worse, she was unable to pass urine. Miss Cooke was left in her hotel until October 15, when she was moved to the National Temperance Hospital.

Dr. Colin Smith, the registrar who examined her, decided she was either about to abort or had had an incomplete abortion, and that she was becoming dehydrated from vomiting. On October 16 Dr. Smith carried out an operation and confirmed his diagnosis of incomplete abortion. He then started to treat her for failure of the kidneys.

Following his discussion with the patient, Dr. Smith got in touch with Dr. Newton and asked for further information. "You may be surprised to learn when that happened that Dr. Newton denied that he had aborted the woman. He said she had come to him with recent influenza and menstrual irregularity and all he had done was to give her some tablets and he had sent her away," said Mr. Seaton. Dr. Newton admitted later that he had attempted to procure the abortion of Miss Cook by the injection of utus paste. He also corroborated what Miss Cook had said —namely, that at the time of the injection she suffered considerable pain.

For a time Miss Cook responded to treatment, but on October 24, when everybody thought she had got over the worst and she was talking to a sister and a nurse, she just died.

Statements by the Defendants

In the meantime, on October 22, Mr. Longstaff, a friend of Miss Cook, went to the police, and in consequence Dr. Newton was seen by a detective inspector. Dr. Newton at once admitted that he had treated the woman with a view to terminating her pregnancy. "She was sent to me by Dr. Stungo," he added.

In a statement Dr. Newton said he was an obstetrician and he specialized in women's diseases. "On October 11, during the morning, I was telephoned by Dr. Stungo," he said. "He told me he had with him a Miss Cook, who was in a poor state physically and she had been sent to him by Dr. Sugden. He said this woman had been sent to Dr. Sugden by Dr. Parsons. Dr. Parsons had said this lady was pregnant and was mentally ill and that in his opinion her pregnancy should be terminated. Dr. Sugden had examined this woman and had said she was about three months' pregnant. In view of her mental condition he referred her to Dr. Stungo. Dr. Stungo said he had examined her and he thought her condition was rather urgent in view of her mental outlook and said he was sending her to me for my opinion. I made an appointment to see Miss Cook later in the day. She was a thin, pale, and very worried-looking woman. She accounted for her pale state by severe influenza. She said the man she had come

to marry had taken most of her possessions and had left her. She was in a desperate condition. She said she was going to throw herself into the river. In view of her general demeanour and the views of the aforementioned psychiatrists I decided to terminate her pregnancy. The question of a fee was discussed, and, in view of the fact that I might have to look after her for some time, I told her it would be £75. This she agreed to. I decided it would probably be best if the uterus was emptied as soon as possible. I gave her an injection of 'achromycin' (tetracycline) and a utus injection. I gave her a prescription for achromycin capsules. She paid me in cash before she left. I visited her on the following Saturday, Sunday, and Monday at the Mapleton Hotel. She told me she had pain in her lower abdomen, but from her story it was difficult to determine whether or not she had had an abortion. . . . On Monday, October 14, I found her much weaker, so I decided to send her into hospital for further examination and treatment. I did not mention that I had given her the utus paste but said she had had a miscarriage. I didn't know whether she had aborted or not. . . . I have handed you a certificate which I received from Dr. Stungo."

On October 24 Dr. Stungo was seen by the police. He said he came to the conclusion that Miss Cook was in a distressed state and he sent her to Dr. Newton for any help he could give her. In a statement he said :

"On October 11 I was spoken to by Dr. Sugden. He said a nurse had been sent to see him by Dr. Parsons. He told me she was in a disturbed emotional state and in a poor physical state. He thought something would have to be done for her. . . . I said I would see her and made an appointment. Miss Cook came to see me on October 11. She told me she was an Australian and that she had come to this country on the expectation of marrying a man aged 57. She had been intimate with him and believed she was pregnant. . . . She told me she had had 'flu and was very distressed. She looked ill. . . . She said she could not go on living as things were. Miss Cook said she could not go back to Australia and she was quite frantic. In the circumstances I deemed it necessary for something to be done for her, and that in my opinion the pregnancy would have to be terminated. I only came to this decision after long discussion with her, and when I had used every endeavour to paint the picture in different colours. I decided to send her to Dr. Newton. . . . She paid me three guineas as a fee."

Mr. Seaton said: "What the Crown suggest is that this was a convenient set-up under the cloak of medical attention whereby the law is dodged. You can say someone is mentally distressed and therefore the pregnancy should be terminated. You send the woman from one doctor to another, who eventually does it for £75." Dr. Newton did not carry out the operation in a hospital, but in his consulting room for £75, and when eventually the patient was sent to hospital he lied. If this were a proper therapeutic operation because her life or mental health were in danger, then why the secrecy ? Why behave in the way these defendants behaved when this operation was carried out ?

Medical Evidence

Dr. Colin Smith, in evidence, said he came to the conclusion that Miss Cook was suffering from some kidney failure 24 hours after her admission to hospital.

Mr. Gerald Howard (defending Dr. Newton): "You will agree that death was due to renal failure ? "—"I think it was in consequence of renal failure. I think the actual cause of death is exceedingly difficult to explain away. Why the patient should be all right at five minutes to seven and dead at five minutes past seven is exceedingly difficult to explain."

"If the heart had to deal with a considerable excess of fluid she might die suddenly ? "—"One would expect to have some signs that she was getting worse."

"Did you at any time ask Dr. Newton whether utus paste contained any mercury ? "—"That was one of the reasons I asked him to come and see me. Had we established she had anuria from mercury intoxication we might well have sent her to Hammersmith, where they have an artificial kidney. I think Dr. Newton said he had not realized that utus paste contained mercury. Beyond that I cannot recollect what was said."

Dr. Smith was then cross-examined by Mr. Norman Richards on behalf of Dr. Stungo. He agreed that he called in Dr. A. G. Spencer, of University College Hospital, to see Miss Cook. One of Dr. Spencer's observations written down on Miss Cook's chart was "? desire to live." Dr. Smith also agreed that Dr. Spencer had described Miss Cook's general condition as inexplicably poor.

Mr. Richards: "If you were examining a patient who had been sent to you by another doctor would you pay regard to what the other doctor had said, and to the notes he had made ? "—"Yes, I would."

"But if you had to carry out an operation would you be the one who would make the final decision ? "—"Yes."

Mr. Beaton (in re-examination): "Did you think that Miss Cook had the will to live ? "—"I think she did. She discussed her work and what she intended to do when she got better."

Dr. F. E. Camps, who conducted the post-mortem examination, said in evidence that the cause of death was renal failure following upon an abortion. Answering Mr. Seaton, Dr. Camps said in his view an operation for termination of pregnancy should always be carried out in hospital.

Mr. Richards, cross-examining Dr. Camps, asked him about the number of unmarried women who committed suicide during pregnancy. Dr. Camps replied that in the part of London for which he was responsible about five women a week committed suicide, or just over 200 a year. Of that number not more than five were pregnant. Dr. Camps agreed that in a book he had written he had said that it was in the third month that an unmarried pregnant woman became desperate.

Mr. Justice Ashworth: "Will you assume that you have got an unmarried and pregnant woman apparently threatening to commit suicide. She is seen by a psychiatrist in the morning and operated upon that afternoon in Harley Street. At the time she is living on the fifth floor of a hotel in Coventry Street. I gather the abortion will not take place immediately. Would you let the woman go back to that hotel to go through that abortion alone ? "—"I personally would not."

"Would there or would there not be any risk involved ? "—"I think there would have been an unjustifiable risk."

Prosecution's Expert Witnesses

Mr. R. A. Brews, gynaecological surgeon at the London Hospital, said in his opinion there was always a great risk in terminating a pregnancy, even in the best possible circumstances. He had twice used utus paste in performing operations, but that was 15 years ago. "I was so dissatisfied with the risk that I have not used it since," he said. If he did use utus paste he would regard it as a surgical operation, and it should be carried out in the operating theatre of a hospital. After the operation the patient, if she had been three months pregnant, would be kept in hospital for five or seven days.

Mr. Seaton: "If you had a request to terminate a pregnancy from a psychiatrist would you act upon it as it stood without further bother ? "—"I should insist that the patient be seen by one of my intimate colleagues in my own hospital, someone whose judgment I respect." The trial was then adjourned, and Mr. Brews continued his evidence the next day (Thursday, May 15).

Mr. Seaton: "As a medical man, if you had a patient with suicidal tendencies would you leave her to her own devices in the West End of London ? "—Mr. Brews: "No, sir."

Mr. Justice Ashworth: "One of the matters which the jury may have to consider has been put in this way, 'Whether a doctor acted in accordance with a practice accepted as proper by a responsible body of medical men skilled in that particular art.' You may know the quotation. I want to put to you an assumption and then I would ask you to comment on it in the light of what I have just read out. Dr. Newton in his statement said he found that Miss Cook was tender in the lower abdomen,

the uterus was enlarged to the extent of about 2½ months pregnancy, there was in addition a bloody discharge from the cervix which indicated a possible infection in the uterus. Dr. Newton decided it would probably be best if the uterus were emptied as soon as possible to get rid of any infection that might be present. He gave her an injection of achromycin. . . . That was his description of what happened in his consulting-room." The judge then asked Mr. Brews: "What is your view of that procedure in the light of what I have just read?" He replied: "I cannot agree that the procedure described here conforms with a reasonable standard of medical practice."

Judge: "Now I come to the second stage. Dr. Newton in his statement says, 'I told her to go to bed. I visited her on the following Saturday, Sunday, and Monday. . . . When I visited her first on the Saturday she was being sick. She told me she had pain in her lower abdomen, and from her story it was difficult to determine whether or not she had had an abortion. . . . On the Sunday I found her condition much the same, on Monday I found her much weaker and the vomiting was still continuing, so I decided to send her into hospital for further examination and treatment. . . . I would say that at this time I did not know whether she had aborted or not."

Judge: "Have you any comment to make in the light of what I read out to you just now?"—"I think the situation of the patient would have been safer if she had been under complete hospital or nursing-home supervision during the whole of that period. I could not accept the practice as outlined here as proper."

Mr. Howard: "Assume that this woman had refused to go into hospital or a nursing-home and that she was determined that no one more than could possibly be helped should know about her condition, that puts a medical man in a difficult position does it not? I mean if the doctor is convinced that there is a danger to her life if he does not do something by way of removing the pregnancy."—I cannot say that such a difficulty would justify a doctor in carrying out a procedure which also unnecessarily endangered her life."

"In your view he should have sent her away and taken the risk of her committing suicide?"—"I do not think the risk of her committing suicide was any greater by sending her to hospital than in letting her go home to a hotel."

"I think we have agreed that the best judge of the condition of the woman and the various risks must be the persons who saw her."—"You asked me what I thought I should do if there was a risk of suicide."

The next witness was Sir Paul Mallinson, consultant psychiatrist to St. George's Hospital.

Mr. Seaton: "Do you sometimes have patients referred to you who are pregnant and are considered to have suicidal tendencies?"—"Yes. That is one of the most difficult symptoms. . . . I would endeavour to persuade the patient to go into hospital."

"What is the practice when you have decided that a termination of pregnancy is desirable?"—"As a rule the psychiatric urgency of such problems is not very great and it is usual to write back to the family doctor recommending termination and giving one's reasons and then leaving the arrangements for the termination to be made in the local hospital. . . ."

Mr. Richards: "You have never had experience of having an unattached, lonely, single woman coming to consult you without coming through another doctor?"—"No."

"Would you refuse to see her?"—"Yes."

Reading from a letter in the *Lancet*, Mr. Richards quoted, "One of the most difficult and vexatious problems which confront the psychiatrist is how seriously to take threats of suicide in women with unwanted pregnancies. On occasion these threats are expressed in the hope that they may constitute grounds for therapeutic abortion and have no validity whatsoever. But very often they are the anguished cries of desperate women with the definite intention of taking their lives as an alternative to abortion." Mr. Richards then asked the witness: "Do you agree with that?"—Sir Paul: "I do not agree that it is very often."—Mr. Richards: "Would you substitute sometimes?"—"Yes."

Reading again from the *Lancet*, Mr. Richards went on: "So many lives are lost by suicide which doctors have no opportunity of saving, because they were never consulted, that it behoves them to give their most careful attention to patients threatening it. Certainly the risk must never be underestimated because the intention has been expressed." Counsel then asked witness: "Do you agree with that?" and Sir Paul replied: "Yes."

Mr. Richards: "A carefully considered opinion is there expressed?"—"Yes."

Mr. Richards: "They are the observations of Dr. Stungo and appeared in the *Lancet* in 1951."*

Detective Inspector L. Godbold was the next witness and he gave evidence of taking statements from Dr. Newton and Dr. Stungo and serving on them the warrants for their arrest. That concluded the case for the prosecution.

Dr. Stungo Discharged

In the absence of the jury Mr. Richards then submitted that there was no evidence for the jury to consider as far as Dr. Stungo was concerned. "The Crown have to establish *mala fides* and I submit there is not one iota of evidence of *mala fides* established," counsel told the judge. "What evidence there is of the condition of Miss Cook is favourable to the accused. . . . All the evidence is in favour of this woman being in such a state that a medical practitioner could come to the conclusion, which might be wrong, but which would be a genuine conclusion. That is not this case. The Crown have to prove that Dr. Stungo acted *mala fide*. Here is a doctor who keeps the fullest possible records of his patients and no one has suggested that his fee of three guineas was excessive. After the testimony of Sir Paul Mallinson I submit there is not that degree of evidence which amounts to a sufficiency in law."

Mr. Howard then made a similar submission on behalf of Dr. Newton.

Judge: "What bothers me in Dr. Newton's case is that he did not tell the truth. The consideration is different in his case. One doctor may recommend a termination of pregnancy, but it is for the surgeon to make up his mind. Then he denies it, why?"—"It may be for a variety of reasons. A man can, quite consistent with innocence, arrive at the view that pregnancy should be terminated, and terminate the pregnancy, and then lose his head afterwards."

"Mr. Howard, I shall be against you, even if I am with Mr. Richards."

After the luncheon adjournment the judge said, "I have considered the whole of the evidence so far as Dr. Stungo is concerned, and in my judgment the submission of Mr. Richards is properly made and I rule that there is insufficient evidence. More than that I do not think it right to say."

The judge thereupon directed the jury to return a formal verdict of not guilty in the case of Dr. Stungo and he was discharged.

Dr. Newton's Evidence

Dr. Newton then went into the witness-box. He said he specialized in endocrinology and did not practise under the National Health Act. On October 11 Dr. Stungo, whom he had known as a psychiatrist for eight or nine years, telephoned him about Miss Cook. Dr. Stungo told him that she had suicidal tendencies and that he thought her pregnancy should be terminated. "Dr. Stungo told me this woman had a very unhappy history and was likely to commit suicide at any time. He had tried to persuade her to go into hospital, and said she had been seen by Dr. Parsons and Dr. Sugden. She was opposed to going into hospital because she said there were many Australian nurses in London hospitals and nursing-homes and she was extremely afraid of being recognized. Dr. Stungo reiterated his opinion that the pregnancy ought not to be allowed to go on."

Dr. Newton said Miss Cook came to see him at 2.30 the same afternoon. She appeared extremely depressed and anxious and despairing of the way life had treated her. "She told me she was alone in this country, she had no

Lancet, 1951, **2**, 1091.

relatives or friends here and no one to turn to. She was unwilling to go back to Australia in her condition as Australia was rather provincial in its outlook and she could not bear the thought of carrying that burden. She said she would rather take a dose of sleeping-tablets or throw herself into the river," Dr. Newton went on. "She told me her previous history, that she had been engaged to be married to an airman who unfortunately was shot down and killed. She suffered a great disappointment in her life because of that. She told me she had been in a sanatorium for a year with pulmonary tuberculosis and that some time ago she met a sailor of whom she grew very fond. She said she had come to this country with the intention of marrying the sailor and they had had intercourse on her arrival. Subsequently she found out that he was already married and he had obviously let her down. She was a nursing sister and not a promiscuous type of woman, and she felt her life was completely spoilt. She looked rather ill and she told me amongst other things that she had had influenza about ten days previously. It was possible that post-influenzal depression was making her more depressed than usual, but I had no means of assessing that."

Mr. Howard: "Did you examine her physically?"—"Yes. She was rather difficult to examine. She was much more tender than the average woman. I came to the conclusion she was two and a half months pregnant. There seemed to be a bloody or serous discharge from the cervix. That was rather unusual and suggested to me the possibility that there had been an attempt to produce a miscarriage. To my mind that was unusual in a nurse, who might be expected to know something about the subject. I took her temperature and pulse and they were quite normal. I listened to her chest and took her blood pressure. I had reason to believe she had had influenza, and that might have accounted for her rather pale complexion, but there were no signs of illness at that particular time."

"Had you got the letter from Dr. Parsons?"—"Dr. Stungo had given me the letter in the lunch hour. Dr. Stungo's general explanation was very much longer and more detailed than the letter. Besides which I did not know Dr. Parsons except that Dr. Stungo had told me he was a psychiatrist."

"Apart from that, did you form an opinion on your own?"—"I thought she was definitely suicidal. I thought that left alone she might quite easily have done something desperate to herself."

"Was anything said about her having the baby?"—"I told her there were facilities for adoption and the possibility of her going home to Australia and facing up to the situation. She said she would rather do away with herself than face the shame."

"Was anything said about getting her into hospital or a nursing-home?"—"When I made up my mind that hospital was the right thing to do, I offered to try and get her into hospital or, failing that, into a nursing-home. She was adamant. She refused to go into any institution. She was afraid of being recognized. She thought too many people would get to know about it. She reiterated that she was a nursing sister of long experience and was quite capable of looking after herself. I first examined Miss Cook at 2.30, and, having come to the decision which I did, I said to her, 'Go away and think about the situation. If you feel the same way, come back and talk to me later in the day.' She returned at 5.30. She still maintained that she could not face having the baby and was going to do away with herself. She still refused to go into hospital or a nursing-home, and, in view of the fact that there was this prospect that she might do something to herself, I decided to operate. I performed an operation to terminate her pregnancy in my consulting-room."

Judge: "Was anyone else present?"—"No, it was not necessary for anyone else to be present. I agree it would have been better, but I have been used to working on my own for many years, and this was a comparatively simple procedure."

Mr. Howard: "You used utus paste?"—"Yes."

"Had you any idea that utus paste might damage the kidneys?"—"I had never heard of such a thing."

"Did she suffer any pain?"—"Not to start with, but towards the end of introducing the paste she did complain of some pain. As there was tenderness in the first place I was not surprised that she complained of some pain."

"Dr. Smith says you had to give her pethidine to relieve the pain?"—"I certainly gave her pethidine, but it was not intense pain. I am afraid Dr. Smith's recollection of the conversation is somewhat hazy."

"After you had injected the paste did you give her anything else?"—"Yes, 250 mg. of achromycin. That is a prophylactic against possible infection."

"Why did you do this operation if you thought there might be some infection?"—"There were several factors to consider. The possibility of her committing suicide. . . . I had to decide which was the best course to adopt in her interests."

"Why did you think it was necessary to do it at once?"—"I thought she was sufficiently suicidal. If left alone she might easily have carried it out. In addition there was Dr. Stungo's view that she required urgent attention and that had quite an influence on me."

"Did you balance the various risks in your mind?"—"Yes."

"Why did you let her go back to the hotel alone?"—"I put her in a taxi. There was no other course open to me. She refused to go into hospital; it was the only course. I told her to stay in bed and if she needed help she was to telephone me. She also said there was adequate help at the hotel."

"Did you discuss the matter of payment?"—"Yes that was done at 2.30 p.m. I told her the fee would depend on how much work I had to do. I said I would probably have to visit her seven times after the operation and that my fee would be £50. I said if there were any further treatment it would be another £25 because I had no means of assessing how long she might require attention."

"Did you regard that as an excessive fee?"—"I purposely put the fee at a high figure compared with what one would normally charge a nursing sister, in an attempt to discourage her from having anything done. As she was staying in a hotel and there was no one I could refer to, it was not an unreasonable procedure to accept the fee in advance."

After the Operation

Dr. Newton then dealt with his visits to Miss Cook at her hotel after the operation. On the first visit she said she thought she had lost the foetus but she did not know whether she had had a complete abortion or not. Her temperature and pulse were normal. On the Saturday (October 12) she was completely free from pain. "I found nothing which in my view showed any cause for alarm," Dr. Newton added. On Sunday she complained of nausea. "I took her off the achromycin capsules because they occasionally cause nausea and vomiting. So far as I was able to tell there was no cause for alarm on that day." On the Monday, October 14, she was vomiting rather persistently, although her temperature and pulse were normal. She complained of tenderness in the stomach, she was constipated, and Dr. Newton said he decided to send her into hospital. She still did not want to go to hospital and said she would be all right in a day or two. On the Tuesday she was taken into hospital. "I had come to the conclusion she had some retained products and the womb required emptying," he said. From then on Dr. Newton said he kept in touch with the hospital daily. "Dr. Smith telephoned. He said Miss Cook was ill and he was rather disturbed about her condition. He told me Miss Cook had said I had given her an injection to procure an abortion, and we discussed the composition of the paste. He also said she had developed anuria and he wondered if the paste had anything to do with it. He asked whether it contained mercury. . . . I never denied to Dr. Smith that I had performed an operation. Then Dr. Smith said I should go and see him and have a chat about the matter. That was on October 19."

Mr. Howard: "Did you come to the honest opinion that it was necessary to perform this operation on this girl because you thought she was liable to kill herself?"—"Yes."

"Under the circumstances in which you were placed did you take all proper steps to perform the operation?"—"Yes."

Dr. Newton's Cross-examination

Mr. Seaton then cross-examined Dr. Newton.

Mr. Seaton: "If you had got this girl into hospital that would have been the end of your fee of £75."—"Firstly, the fee was £50. Money was never a consideration here. If I had wanted £50 or £75 I would never have let her out of my surgery."

"This could have been done under the National Health, could it not?"—"Yes, if the patient had been willing to go to hospital."

"Are you always alone when you carry out operations?"—"Yes, the operations I undertake are always minor ones."

"Was this a minor operation?"—"In its technique, yes."

"This is an operation in which there is grave risk, is there not?—"I consider, if normal precautions are taken, there is no more risk than there would be if it were done in the most elaborate theatre."

Judge: "That is not an answer to the question. Wherever it is done termination of pregnancy is fraught with risk?"—"Yes, any curettage is fraught with risk."

Mr. Seaton: "The injection of utus paste is a risk. Isn't it wise to have someone to assist you in case of mishap?"—"If one went through life like that no doctor would risk giving an injection to anyone. I regarded that as a comparatively simple procedure."

"Sometimes with utus paste you get an air embolism?"—"I don't think so. If there were that risk I do not think the thing would be allowed to be sold."

"And there is the risk of shock?"—"I think there is a risk of shock if you inject too much. I should think the risk of shock was minimal."

Judge: "This woman was ill, wasn't she?"—"I thought she was in poor condition."

"That would increase the liability of shock?"—"It is a possibility, not more."

Mr. Seaton: "What steps did you take to reduce the risk of shock?"—"None."

"With a tender cervix what steps did you take to cope with flinching on the part of the patient?"—"I did not anticipate any flinching."

"I suppose if the patient moves there is a danger of penetrating the wall of the uterus, and if you did that it would be quite disastrous?"—"Yes."

"At the inquest on Miss Cook you described the discharge as pussy. That indicates the possibility of sepsis. What steps did you take to see if there was sepsis?"—"None."

Judge: "It was a bit risky to proceed with this operation without making sure?"—"Yes."

"If you carry out that operation and it happens there is sepsis, that might result in the woman dying. Did you think it worth while chancing your arm with the patient rather than waiting three or four days for a pathological test to be made?"—"One has to assess that against the possibility of suicide the next day. I think the risk of infection was minimal."

Mr. Seaton: "Did you think it right to get something in writing from the patient before performing the operation? Her consent, I mean?"—"That aspect of it never entered my mind."

"Did you ask Miss Cook to retain what came away?"—"I did."

"Then can you explain why this trained nurse put it down the lavatory?"—"That is what she did."

The trial was then adjourned till Friday.

Continuing his cross-examination, Mr. Seaton asked Dr. Newton what he had prescribed when he called at Miss Cook's hotel the day after the operation (Saturday).—Dr. Newton: "I didn't prescribe anything. She was saying she was feeling on the sick side and she could keep down soda water, and I said, 'Keep on with that.'"

"What of her condition on the Sunday?"—"She was more or less the same as the day before. She said she felt sick. Against that there was normal temperature and pulse. There was no complaint of pain. There was no haemorrhage or discomfort down below."

"Did she tell you she had urinary trouble?"—"No, she said she was constipated and I gave her something for it."

"What else did you do?"—"There was nothing else to do. I expected the nausea and vomiting to subside." In reply to another question Dr. Newton added: "She had been vomiting before she came to see me. Vomiting can be of nervous origin."

"In view of the persistent vomiting had you in mind dehydration?"—"I did not have that in mind. I wasn't looking for that."

"And by the Sunday (October 13) you knew the placenta was still in the uterus?"—"No, I thought the thing had completely gone. I did not think that the abortion was anything but complete. One would have expected, if she had had an incomplete abortion, to have had some signs of haemorrhage down below, one would have expected a raised pulse rate and temperature. I had no reason to believe she had any retained products."

Judge: "When did you first come to the conclusion that the products might be retained?"—"On the 14th."

Mr. Seaton: "In your statement you say, 'On October 14 I found her much weaker and the vomiting was still continuing so I decided to send her to hospital for further examination. . . .' When did you take steps to get her into hospital?"—"On the Tuesday."

"So you let another 24 hours go by?"—"She said she thought she would be all right and she would not go."

"Why did you let that woman lie in that hotel getting weaker and weaker for another 24 hours?"—"I was still guided by the absence of clinical symptoms."

Judge: "If she had been willing would you have sent her to hospital on the Monday?"—"Yes."

"Because she was in danger?"—"I cannot say danger. She looked more ill."

Mr. Seaton: "Did it occur to you to get another opinion?"—"I certainly would have done so if she had had any clinical symptoms. I didn't think she was that bad."

"There was no doubt about it, she was getting worse, wasn't she?"—"Yes."

"And rapidly worse?"—"Not rapidly worse."

"It was most urgent that she should have a clinical examination?"—"As it subsequently transpired. I possibly made an error of judgment."

Judge: "It goes further than that. On the Monday you had formed the view that there was something inside her which ought not to be there, and which had to be removed. That meant hospital. The longer she remained (in the hotel) the worse she would be"—"Yes."

Asked about the letter he sent to the hospital when Miss Cook was admitted, Dr. Newton agreed that he did not disclose that it was he who had carried out the operation. "I stated what I thought was wrong with her," he added.

Mr. Seaton: "You could have put in the letter 'I have treated this patient for termination of pregnancy with utus paste. I think she has had an incomplete abortion.' Why didn't you say that?"—"I wrote the letter in a hurry."

"If Dr. Colin Smith (of the Temperance Hospital) is right when he telephoned you were still not admitting that you were the person who had aborted this woman?"—"Dr. Smith is under a misapprehension."

"Dr. Smith says it was not until you went to see him that you admitted what you had done?"—"That cannot possibly be right in view of the fact that I had discussed the utus paste with him when I spoke to him on the telephone."

"Looking back on the matter now do you agree that your treatment of the patient was obviously utterly inadequate?"—"I was mistaken in my diagnosis early on."

"It is a rule of professional etiquette that when you examine a woman, particularly her private parts, you should always have someone with you?"—"It is usual."

"Why didn't you follow that?"—"I haven't had a nurse with me for several years. There is a woman just outside my consulting-room door and I have always worked that way."

"When this woman got steadily worse you kept her in a hotel for five days. Was that for concealment?"—"I had no thought for concealment. I thought she was taking time to recover."

Expert Witness for the Defence

The next witness was Professor J. C. McClure Browne, professor of obstetrics at the Postgraduate Medical School of London. He said he had used utus paste on about eight occasions as far as he could recollect. It produced no ill-effects, but in about half the cases surgical evacuation of the uterus was necessary. Questioned about the practice of a doctor always having a nurse or someone else present when examining a woman patient, especially her private parts, he said that was customary, but unfortunately the rule was sometimes broken in private practice.

Mr. Howard: "What do you say with regard to Dr. Newton's description of the way he did the operation?"—"I think his technique, as he described it, is perfectly reasonable."

"Was there anything in your view grossly negligent about what he did?"—"Having regard to the circumstances I do not think this was grossly negligent." Answering a further question the witness said that, provided the patient was co-operative, the insertion of the utus paste was simple.

"What do you say about Dr. Newton letting Miss Cook go back by herself to her hotel?"—"Personally I would have preferred to do all this in hospital, but we did hear that the woman wouldn't go into hospital. From what I have heard I think he was in a difficult position and I can well understand how he came to arrive at the decision he did. I am not saying I would do the same."

"Would you regard that as being grossly negligent?"—"No."

"In your opinion was it grossly negligent not to diagnose anuria?"—"It is very difficult in the early stages in this particular situation to recognize anuria, and I can understand somebody failing to recognize it."

"If anuria is not recognized, in your view would the mention of utus paste in any communication to a hospital be vital or not?"—"No."

"We have been told by Dr. Newton that the patient was worse on the Monday but she refused to go into hospital and he waited another day. What do you say about that?"—"I think if he had not recognized anuria, then on the whole it was fairly reasonable to leave her until the following day. I think had there been haemorrhage he would have been well advised to take some action on that particular day, but in the absence of haemorrhage I do not think it was all that urgent."

Mr. Seaton (in cross-examination): "If you had terminated a pregnancy and another doctor had asked you what you had done, you would not hesitate to tell him, would you?"—"No."

That concluded the evidence for the defence.

Closing Speeches

Mr. Howard, in his final speech on behalf of Dr. Newton, told the jury that the great bulk of the evidence concerning the state Miss Cook was in, prior to the operation, was that she was in a state of acute anxiety. "You may think it difficult to imagine two more relevant witnesses as to the state of this woman's mind than Dr. Parsons and Dr. Sugden, but the prosecution have not thought fit to call them," commented counsel. "They both formed the view that her pregnancy should be terminated, and so did Dr. Stungo."

Criticism had been made that Dr. Newton performed this operation in his consulting-room. Everyone agreed that it would have been better for it to have taken place in hospital or a nursing-home, but Professor McClure Browne had said he had come across a number of cases where patients had taken the same attitude as Miss Cook and had refused to go. "What is to be done if a doctor honestly thinks he should carry out an operation?" counsel asked. "Because one doctor would not do an operation in a certain place and another one did, it does not follow that one of them was negligent, still worse, grossly negligent." In conclusion Mr. Howard added: "Dr. Newton was balancing the risks. He may have been wrong, but in my submission, even if you thought he was wrong, that is a very long way from saying that he was grossly negligent in the sense of being criminally negligent."

In his final speech for the Crown Mr. Seaton said: "What we suggest is that the evidence discloses an illegal operation . . . . and when things went wrong Dr. Newton did everything he possibly could to avoid discovery, and it is because of doing that that he disregarded the skill that he should have displayed in the course of exercising his professional services, that he neglected to do that which he ought to have done for that girl which, together with the result of the illegal operation, brought about her death. . . .

"You have to decide whether when this operation was performed it was performed in bad faith. You have to decide whether all the talk about suicide was a lot of moonshine and whether this operation was carried out for the sake of getting £75 to put in his own pocket and to suit the girl's convenience."

Judge's Summing Up

Summing up, Mr. Justice Ashworth told the jury: "When this case started last Wednesday morning you were told that it was unusual and important, and so it is. It is important and indeed of crucial importance to Dr. Newton, charged as he is with crime, and crime in his professional capacity. And it is important too from the point of view of the Crown, because if you take the view that this is a case of criminal abortion you may well agree that criminal abortion is more sinister and more difficult to detect when it takes place in the high places of Harley Street than in the drab surroundings more usually associated with the crime."

Dr. Newton was charged with using an instrument with intent to procure a miscarriage and he was also charged with manslaughter. In substance there were three charges because the manslaughter charge was divided into two parts. It was said by the Crown that he caused the death of Miss Cook by unlawfully using an instrument, and that he caused her death by criminal negligence.

Considering the first question—Did Dr. Newton unlawfully use an instrument?—the judge said that matter was simplified to a slight extent because there was no dispute that he did, and there was no dispute that he used it with intent to procure a miscarriage. The emphasis was on the word unlawful, and that was the crux of this question. The law on the use of an instrument for such a purpose was this—that it was unlawful unless the use was made in good faith for the purpose of preserving the life or health of the woman.

Health meant not only physical but mental health as well. There might be cases of a woman going to a doctor in a state of great emotional upset, distraught, and verging on the fringe of insanity. If in such a case a doctor said, "If I let this go on and I let her proceed to deliver she will be a mental wreck, if not dead," and he then relieved the woman of her pregnancy, he committed no crime. But, said the judge, "There is no immunity for doctors in the operation of the criminal law, and if a doctor decides to terminate a pregnancy merely in order to oblige the woman, or to relieve her of embarrassment, or for a substantial reward, if it is merely for that, then he is just as guilty of the criminal offence of abortion as would be the woman in a back street."

The jury would appreciate from their knowledge of the world that one of the temptations that a doctor had to overcome was that presented by an anxious and embarrassed woman who wished to be relieved of a situation into which her indiscretion might have led her. "He must resist that temptation, and, unless he acts in good faith for the purpose of preserving her life or health, he ought to send her away," said the judge.

In the present case it was not the physical health so much as the mental health of Miss Cook that was in issue. In the ordinary way a doctor or a surgeon practising his ordinary profession was not expected to be an expert in psychiatry. Accordingly, as the jury had heard in this case, it was the practice, when a woman's mental health gave rise to doubt, to call in the aid of a psychiatrist. Mr. Brews and Professor McClure Browne had both said that it was their practice to call in a man of standing in whom they had confidence. So, in the same way, Dr. Newton had said, "I acted here on the recommendation not merely of one psychiatrist, Dr. Stungo, but also I was armed with the report of Dr. Parsons."

If the jury came to the conclusion that Dr. Newton did unlawfully use an instrument, then they would have to consider whether he thereby caused the death of Miss Cook. Manslaughter had been defined as the unlawful killing by one person of another without any intention to kill. The crime could be committed in many ways. "The one with which you are concerned, and the principle I am about to explain to you, is this," said the judge. "If a person, in the course of or as a result of carrying out an illegal operation, causes the death of the woman, then he is guilty of manslaughter. . . . The fact that in this case death ensued 13 days after the operation does not mean that it was not caused as a result of the illegal operation. The time interval is neither here nor there, but the cause must be proved. There must be a direct chain of causation between the operation and the death. If you come to the conclusion that this operation on that Friday was illegal and the woman died on the following Tuesday week as a result of that operation, and as a direct result of it, then you would find him guilty of manslaughter."

Manslaughter by Negligence

The jury would then have to consider whether Dr. Newton caused the death of Miss Cook by criminal negligence. That was quite independent of the previous two questions. The manslaughter alleged here was killing by negligence. In the ordinary way negligence arose in law when someone committed a breach of duty or care which every individual owed to everyone else. Negligence had been described as the failure to do what a reasonable man would in the circumstances do, or the doing of an act which a reasonable man, in the circumstances, would not do. The test of whether it was negligent or not which the law applied in ordinary cases was the standard of the ordinary man, the man in the street. In the case of a professional man the standard of the ordinary man in the street had not the same value. Accordingly, when a man's professional negligence was in issue, then the standard laid down was in effect the standard of professional men. "In order to establish professional negligence in the case of a doctor it is necessary to prove that he acted in a way which was not in accordance with a practice accepted as proper by a responsible body of medical men skilled in that particular art," said the judge. "What that comes to is this, that you will replace the standard of the ordinary man in the street for the standard of a responsible body of medical men."

Of course there might well be divergent views amongst doctors about what was proper and what was not, and there could well be divergent views as to the best method of dealing with this or that situation, but so long as a doctor acted in accordance with a practice which was accepted as proper by a responsible body of medical men then he kept within the law. "What is suggested here is that, by his treatment of that woman at the operation and after, Dr. Newton acted in a way which was not in accordance with the practice accepted as proper by any medical man." The judge then reminded the jury of what Mr. Brews had said on that subject in the witness-box. In order to constitute the offence of criminal negligence such as to give rise to a charge of manslaughter the negligence had to be such that a jury, fairly considering the facts, could say, "This goes beyond a matter between the individuals. This affronts the public conscience, this amounts to a crime." Another way of putting it was this. In order to justify a conviction of manslaughter a jury must be able to say, each one of them, "If I had been there and had seen it or if I had heard all the facts about it, I would have said to myself that man ought to be prosecuted." In other words, was Dr. Newton guilty of that grave degree of negligence which constituted a crime? "If you take that view and you are satisfied that death resulted from the negligence, then, members of the jury, it would be your duty to convict," said the judge.

The judge concluded by capitulating the evidence on the various charges, and the jury retired.

Verdict and Sentence

After considering their verdict for two and a half hours the jury returned into court. The foreman said they found Dr. Newton guilty of unlawfully using an instrument with intent to procure the miscarriage of Miss Cook, and guilty of manslaughter in that he caused her death by unlawfully using an instrument. The foreman said the jury found Dr. Newton not guilty of manslaughter on the grounds of negligence.

Detective Inspector Sidney Bedford said Dr. Newton was aged 52. On July 22, 1928, he was registered as a medical practitioner. He qualified M.R.C.S., L.R.C.P. He then went into general practice in Hounslow and at Portman Place, London, W.1. On November 26, 1942, his name was erased from the *Medical Register*. He appeared before the General Medical Council for offences relating to false certifications. In that case he gave certificates of epilepsy to enable men to evade service in His Majesty's Forces. On November 25, 1947, after five years, his name was restored to the *Medical Register*. For the past six years he had been practising in Harley Street, specializing in endocrinology.

Passing sentence of two years' imprisonment for unlawfully using an instrument, and three years' imprisonment for manslaughter—the two terms to run consecutively, making five years in all—Mr. Justice Ashworth told Dr. Newton:

"In my view this is a very grave case. The day of reckoning has come for you. You must have known what were the dangers to the lives of women on whom you practised this, if there were others. You must have known too what would be the consequences to yourself if you were convicted. This is not the first time that you have broken the law in regard to medical practice. For five years you were suspended for dishonesty. Now comes this. It comes from a man in Harley Street. It is in some ways even more sinister than it is in normal cases. I cannot take a light view of this."

U.S. POLIO VACCINE MANUFACTURERS INDICTED UNDER ANTITRUST ACT

On May 12 a U.S. Federal grand jury charged five American pharmaceutical firms with having monopolized the production of Salk vaccine and with having fixed prices, in contravention of the Sherman Antitrust Act (*New York Times*, May 13). The charges are stated to involve sales of over $53m. worth of vaccine to Federal, state, and local governments between early in 1955 and December, 1957. The defendants named are Eli Lilly & Co.; Allied Laboratories, Inc., and its Pitman-Moore Division; the American Home Products Corporation and its subsidiary, Wyeth Laboratories, Inc.; Merck & Co., Inc., and its Merck Sharp and Dohme Division; and Parke Davis & Co. All the companies deny the charges and state there was no collusion of any kind. The purchases of vaccine were made under the Poliomyelitis Vaccination Assistance Act, which provided for the vaccine's free distribution by the Federal Government to states.

Universities and Colleges

UNIVERSITY OF DUBLIN

SCHOOL OF PHYSIC, TRINITY COLLEGE

At the recent examination held by the University, the following medical practitioners were awarded the Diploma in Gynaecology and Obstetrics:

Miss Mya Mya Aye, J. O. Foohey, F. D. Heelan, Miss Khalida A. W. A. Kayssi, J. D. Le Souef, Miss Shalini Tanavde.

UNIVERSITY OF CAMBRIDGE

The initials of W. K. Douglas were wrongly given in the list of names of the successful candidates for the degree of M.Chir. printed in the *Journal* of April 5 (p. 840).

UNIVERSITY OF LONDON

Professor M. L. Rosenheim has been appointed representative of the University on the governing body of the Board of Trustees for Medical Research in West Africa, and Dr. Sybil Yeates on the governing body of the Waverley, King's Warren, Manorway and Burrage secondary schools.

Dr. R. S. F. Schilling has been reappointed representative of the University on the council of management of the Slough Industrial Health Service Ltd.

The following have been recognized as teachers of the University in the subjects indicated in parentheses: *Institute of Basic Medical Sciences*, Mr. G. W. Causey (Anatomy); Dr. G. J. Cunningham (Pathology); Dr. D. Slome (Physiology). *Institute of Child Health*, Dr. Eleanor M. Creak (Mental Diseases (Child Psychiatry)); Dr. R. E. Bonham Carter (Children's Diseases); Mr. D. N. Matthews (Surgery). *Middlesex Hospital Medical School*, Mr. J. H. L. Ferguson (Surgery). *Institute of Urology*, Mr. J. D. Fergusson, Mr. A. W. Badenoch, Mr. F. R. Kilpatrick, and Mr. Harland Rees (Surgery (Urology)); Dr. J. C. Hawksley

(Medicine (Urology)). *St. Thomas's Hospital Medical School*, Mr. G. K. Harrison (Surgery). *University College Hospital Medical School*, Dr. G. I. M. Swyer (Medicine (Endocrinology)). *Royal Free Hospital School of Medicine*, Dr. Phyllis Wade (Radiotherapy). *Institute of Neurology*, Dr. R. E. Kelly (Medicine (Neurology)).

Medical Notes in Parliament

ANSWERS TO QUESTIONS

Poliomyelitis after Polio Vaccination

Mr. S. P. VIANT (Willesden, West, Lab.) on May 15 asked the Minister of Health how many cases of poliomyelitis recorded in 1957 developed within one month, two months, and three months of inoculation, respectively; and in how many cases the paralysis was in the inoculated limb. Mr. D. WALKER-SMITH stated that there were records that poliomyelitis developed in 1957 in 8 (5 paralytic), 5 (2 paralytic), and 6 (3 paralytic) children in the first, second, and third months respectively after two injections of poliomyelitis vaccine. In one case, which occurred in the first month, the child had paralysis affecting the inoculated limb. As he had indicated during the debate on the supply of poliomyelitis vaccine on May 1, there were several reasons why poliomyelitis might occur in vaccinated persons. It was not possible to identify the reason with certainty in the individual case.

Cremation Certificates

Mrs. HARRIET SLATER (Stoke-on-Trent, North, Lab.) asked the Home Secretary what further recommendations had been or were to be made to medical practitioners for charges for cremation certificates B and C. Mr. R. A. BUTLER stated that the annual report of the Council of the British Medical Association, published in the *British Medical Journal* on April 19, reminded members of the Association's policy that a suitable fee for the completion of either of these certificates is two guineas plus mileage allowance. The Association had informed him that another reminder was included in a bulletin sent last December to hospital consultants and specialists, and that they recently decided again to draw the attention of hospital staffs to their policy in the next bulletin.

Mrs. SLATER asked whether, in view of the fact that there were many different charges, from two guineas upwards, some of which were considered very excessive, it was possible for the Home Office to do something to reinforce the bulletin sent out by the B.M.A.? Mr. BUTLER said they were watching the matter, but in the meantime would like to support the Association's efforts.

Charges for Private Beds

Mr. JOHN HALL (Wycombe, Con.) asked the Minister of Health on May 12 if he would amend the charges for hospital private beds so that the patient was charged only the difference between the cost of a public and private bed. Mr. WALKER-SMITH replied "No." This course would require legislation, and he doubted whether it would be the best way of using any additional money available for the Health Service.

Mr. HALL pointed out that contributors who, for medical reasons, might be caused to occupy private beds were normally entitled to the full benefits of National Health Insurance. Was there not an element of injustice in forcing such persons to pay the full charge for a public bed, which normally they could occupy free of charge, plus a further cost of 5 to 15%? Mr. WALKER-SMITH replied that this method of payment was prescribed by section 5 of the Health Service Act, 1946, and had been followed since. To vary it would require an amendment of that section.

Dr. EDITH SUMMERSKILL (Warrington, Lab.) called the suggestion "retrograde," and said it would lead to the heavy subsidization of private beds, and consequently a great abuse of the Health Service. Mr. WALKER-SMITH would not associate himself with the harsh epithet, but said there were difficulties in the suggestion that were not confined to the legislative difficulty.

Tours in the Tropics Before Consultant Posts

Mr. JOHN TILNEY (Liverpool, Wavertree, Con.) asked the Minister of Health whether, to help ease the medical requirements of Commonwealth territories and to expand the knowledge of tropical medicine and problems among members of the Health Service, he would recommend the proleptic appointments of consultants so that they could do a tour of duty overseas before taking up such appointments. Mr. WALKER-SMITH said he was advised that the Health Service Acts did not permit him to do so, and he was not convinced that what was proposed would achieve the object in mind. He was, however, considering various representations which had been made to him on the subject.

Transistor Hearing-aids.—There has been some technical difficulty in large-scale manufacture, but, if production samples now being tested are acceptable, deliveries will begin soon.

Opticians Bill.—The Opticians Bill was given a second reading in the House of Lords on May 12.

Vital Statistics

Smallpox in Cheshire

Two further cases of smallpox were diagnosed* on May 17 from New Ferry, Cheshire. Virological confirmation had not been reported at the time of going to press, but the clinical diagnosis was fairly firm. The cases were a man aged 53 with a haemorrhagic rash and his wife aged 54 who had an obsolescent and sparse rash. Both live near the isolation hospital at New Ferry to which three cases of smallpox were admitted a month ago (*Journal*, April 26, p. 1011, and May 3, p. 1073). The woman had a history of a mild illness on May 2–3, while the man became ill on May 13. The patients were admitted to New Ferry Hospital the same day.

Week Ending May 10

A general fall was recorded in the incidence of infectious diseases in England and Wales during the week ending May 10. The largest falls in the notifications were 127 for measles, from 3,699 to 3,572, 121 for acute pneumonia, from 425 to 304, 50 for scarlet fever, from 756 to 706, 45 for dysentery, from 816 to 771, 26 for whooping-cough, from 678 to 652.

The largest falls in the incidence of measles were 83 in Lincolnshire, from 203 to 120, 64 in Northamptonshire, from 164 to 100, 54 in Hampshire, from 176 to 122, and the largest rises were 8 in Dorsetshire, from 46 to 114 (Poole M.B. 42), and 66 in London, from 283 to 349 (Islington 102). Only small changes were recorded in the local trends of scarlet fever and whooping-cough. 4 cases of diphtheria were notified, being 1 more than in the preceding week. All 4 cases were notified in Lancashire, 3 in Liverpool C.B. and 1 in Fulwood U.D.

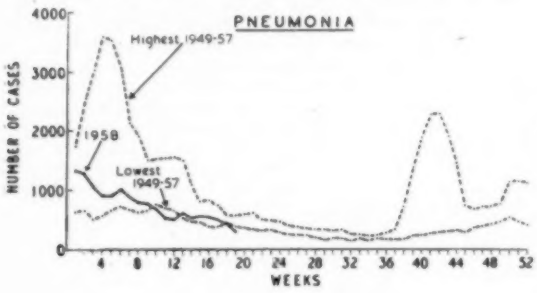
The notifications of acute poliomyelitis numbered 20 and were 2 more for paralytic and 2 fewer for non-paralytic cases than in the preceding week. The largest returns were Yorkshire West Riding 4, Lancashire 3 (Liverpool C.B. 3), London 3.

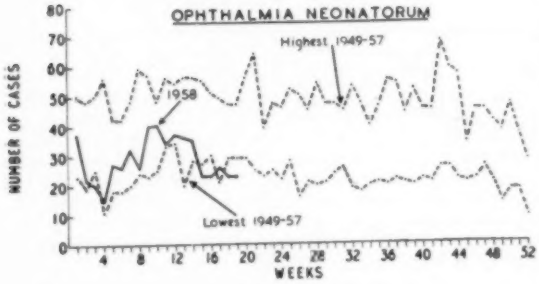
The largest centres of dysentery were Lancashire 189 (Liverpool C.B. 48, Manchester C.B. 37, Oldham C.B. 15, Stretford M.B. 10, Worsley U.D. 10), Yorkshire West Riding 167 (Sheffield C.B. 22, Leeds C.B. 19, Pontefract M.B. 14, Queensbury and Shelf U.D. 14, Bradford C.B. 13, Barnsley C.B. 11), London 74 (Islington 17, Shoreditch 11, Southwark 10), Cheshire 50 (Wallasey C.B. 22, Northwich R.D. 10), Gloucestershire 41 (Bristol C.B. 38), Durham 27 (South Shields C.B. 11), and Berkshire 25 (Easthampstead R.D. 15).

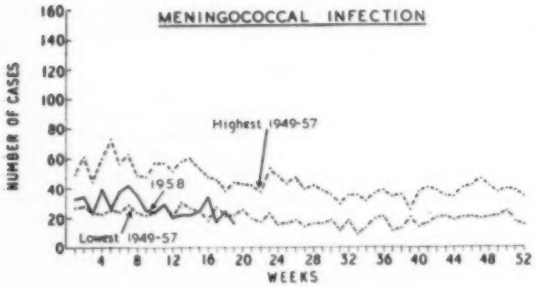
*The death of the man has now been reported.

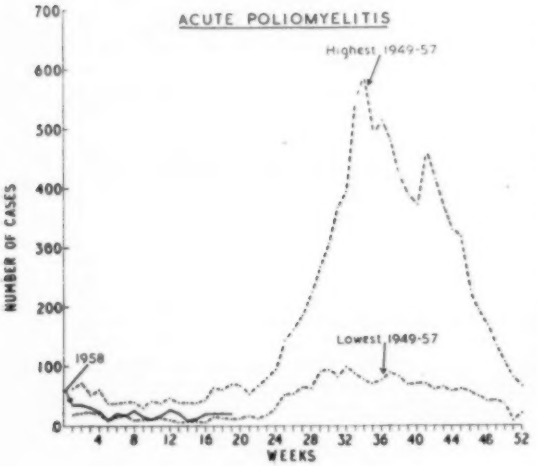
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1949–57 are shown thus ------, the figures for 1958 thus ————. Except for the curves showing notifications in 1958, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **May 3** (No. 18) and corresponding week 1957.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1958					1957				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	3	0	0	0	2	1	0	2	1	
Dysentery	816	100	252	4	7	574	4	233	8	2
Encephalitis, acute	5	2		0		2	0		0	
Enteric fever:										
Typhoid	5	0	1	0	1	2	0	0	0	1
Paratyphoid	2	1	2(B)	0		1	0	6(B)	0	1(B)
Food-poisoning	176	28	27	2		164	17	17	0	
Infective enteritis or diarrhoea under 2 years				9	15				14	13
Measles *	3,699	283	160	63	8	23,188	1640	193	321	229
Meningococcal infection	24	0	6	0	1	25	1	16	2	1
Ophthalmia neonatorum	23	3	3	0		43	5	8	0	
Pneumonia †	425	28	238	6	2	447	35	159	5	6
Poliomyelitis, acute:										
Paralytic	11	3	1	1	4	35	2	4	1	7
Non-paralytic	9	1				25	0			
Puerperal fever §	200	24	19	0		211	34	8	4	
Scarlet fever	756	60	67	22	16	480	33	73	24	21
Tuberculosis:										
Respiratory	646	95	123	16		613	67	383	23	
Non-respiratory	89	3	15	7		100	7	13	2	
Whooping-cough	678	27	50	14	15	2,399	77	228	6	41

DEATHS	1958					1957				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	No comparable figures available.	0	0	0	0
Dysentery	0	0		0			1		0	
Encephalitis, acute		1			0		1			0
Enteric fever	0	0	0	0			0	0	0	
Infective enteritis or diarrhoea under 2 years		0	0	0	0		0	2	0	0
Influenza	23	0	1	1	1		0	0	0	0
Measles		0	0	0	0		1	0	0	0
Meningococcal infection		0	0				0	0		
Pneumonia	527	45	29	4	11		36	18	15	4
Poliomyelitis, acute	4	0		0	0		0			0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	78	8	7	1	4		5	6	1	3
Non-respiratory		0	0	0	2		0	0	0	1
Whooping-cough	0	0	0	0	0		0	0	0	0
Deaths 0–1 year	341	24	31	4	15		28	29	12	9
Deaths (excluding stillbirths)	9,920	724	587	103	180		784	573	111	170
LIVE BIRTHS	14,724	1241	1091	281	387		1212	1105	254	408
STILLBIRTHS	326	23	29				25	27		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Developments at Sheffield.—On May 17 QUEEN ELIZABETH THE QUEEN MOTHER laid the foundation-stone of what is to be the out-patient department of a new teaching hospital at Sheffield. Two days earlier the Lord Mayor of Sheffield, Alderman A. BALLARD, had opened Whiteley Wood Clinic as the main clinical unit of the university department of psychiatry (Professor E. STENGEL). The new teaching hospital, when completed, will be a comprehensive acute general hospital of 800 beds, closely integrated with the University. Its cost has been put at about £4m. After the out-patient department, the next stage will be 250 beds for in-patients. Already built on an adjacent site as part of the total plan is the Charles Clifford Dental Hospital, which opened in 1953. The architects are Messrs. Adams, Holden, and Pearson. The Whiteley Wood Clinic is a conversion of a former rehabilitation centre at a cost of £75,000. It will provide the department of psychiatry with 29 in-patient beds, facilities for the treatment of day patients, and an out-patient department.

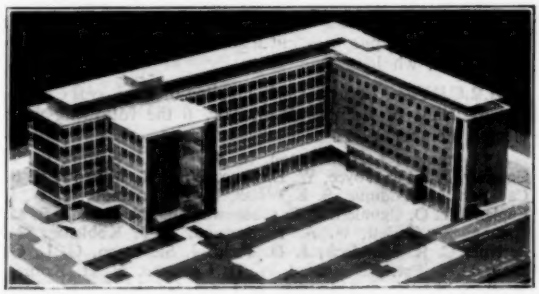
Perth Medical School.—The new School of Medicine of the University of Western Australia was officially opened on April 10 by the State Governor, Lieutenant-General Sir CHARLES GAIRDNER. Teaching at the School began in 1957, when a first-year class of 85 students was enrolled and a sixth-year class of 16 Western Australian students returned to Perth from Adelaide University; at that time, however, the school building had not been completed. By 1959 all six years of the course will be running. Government support for a medical school at Perth being contingent upon a tangible expression of favourable public opinion, an appeal for £400,000 was launched in September, 1955, and within a very short space of time over £500,000 was subscribed. After this, development was fast. The departments of anatomy, physiology, and biochemistry were sited on the university grounds; four of the main hospitals of the metropolitan area were designated teaching hospitals (the Royal Perth Hospital, the Princess Margaret Hospital for Children, the King Edward Memorial Hospital for Women, and the Fremantle Hospital); and the radium block near the Royal Perth Hospital was extended and converted to house the faculty's administrative offices, common-rooms, and laboratories, two lecture theatres, and the departments of pathology and microbiology. The Western Australia Branch of the B.M.A. put its library at the disposal of the faculty, and together they have united to set up a new Medical Library of Western Australia, next door to the faculty building.

Lewisham Hospital.—On May 15 PRINCESS MARGARET opened a new out-patient department at Lewisham Hospital. This is the first phase of the hospital's rebuilding after extensive bomb damage during the war. The cost of the department with its equipment will be about £200,000. The next phase will be the provision of new operating theatres, an *x*-ray department, and a pharmacy, for which Parliament has already allotted £300,000.

Editors of Medical Student Journals.—A conference of editors of British medical student journals, presided over by Mr. MICHAEL S. HALL, editor of the *British Medical Students' Journal*, was held at B.M.A. House on May 10. Some 70 delegates were present to hear talks by Dr. T. F. Fox, editor of the *Lancet*, on editorship; Mr. JOHN HUNTER, of Hazell, Watson and Viney Ltd., on printing; and Mr. M. COZENS, of the Advertisement Department of the *B.M.J.*, on advertisements. The afternoon session was devoted to short opening speeches by various editors, followed by general discussion, on the many aspects of editing. The delegates were entertained to a dinner in the evening by the *Lancet*, at which Dr. Fox took the chair.

M.O.H.s Teaching Group.—The Society of Medical Officers of Health has formed a Teaching Group, under the chairmanship of Professor FRASER BROCKINGTON. The Group's first conference and annual meeting is being held at the Ciba Foundation, London, on June 13 and 14. The main subjects for discussion will be "The Future of the Medical Services and Its Implications for the Teaching of Social Medicine," "The Content of Social Medicine: For (*a*) the Medical Student and (*b*) the D.P.H.," and "Teaching Methods." M.O.H.s and other doctors who would like to participate in this meeting are invited to apply to the Group's hon. secretary Dr. JOHN BURTON, Central Council for Health Education, Tavistock House, Tavistock Square, London, W.C.1.

Middlesex Hospital Medical School.—The photograph below shows the south aspect of a model of a new building for the Middlesex Hospital Medical School, work on which began last December. Sited between Charlotte Street and Cleveland Street, the building will house in the longer arm



of its L the departments of chemistry, physics, biology, anatomy, physiology, and pharmacology, while the shorter arm will provide residential accommodation for 174 students. There will also be lecture theatres, common-rooms, administrative offices, and recreational facilities (squash courts, music room, stage, etc.). £1.5m. is needed for the building and so far £970,000 has been raised. There are plans for a further building scheme to provide accommodation for clinical departments, a library, and a great hall.

Medical Charities.—The B.M.A. has issued a new edition of its booklet *The Charities of the Medical Profession*. The booklet describes the following medical charities and their purposes: the Royal Medical Benevolent Fund; the Royal Medical Benevolent Fund Society of Ireland; the Royal Medical Foundation of Epsom College; the Sir Charles Hastings Fund; the Christine Murrell Fund; the Dain Fund. There is also a note on how to subscribe to the various funds and a bankers order form. Copies of the booklet are available from the Secretary of the Association, free on request.

Widows and Orphans of Medical Men.—The Society for Relief of Widows and Orphans of Medical Men held its annual meeting in London on May 14. Mr. A. RUGG-GUNN took the chair in the absence of the president, Sir ROBERT YOUNG. During 1957 the Society provided over £4,000 to help necessitous widows and orphans of doctors. At the end of the year 25 widows were receiving grants from the Society. Inquiries about membership should be addressed to the secretary, Dr. J. A. STRUTHERS, at 11, Chandos Street, Cavendish Square, London, W.1.

Chelsea Clinical Society.—Sir WALTER FERGUSSON HANNAY presided at the annual dinner of the Chelsea Clinical Society last week. Mr. JULIAN AMERY, M.P., in proposing the health of the Society, said he was once attended in Albania by a doctor 105 years old who insisted upon having lunch and a rest before he gave him an antimalarial injection. Sir WALTER HANNAY said that the Society, with a membership limited to 300, was flourishing, and in this their jubilee year they had elected their first honorary member, Sir Cecil Wakeley. The toast, "The Guests," was proposed by Dr. H. S. PASSMORE, and the EARL OF HALSBURY responded. At the end of the evening the new president, Dr. HARRY COKE, was installed in office.

National Varicose Foundation.—At a reception in London on May 15, sponsored by Messrs. Lastonet Ltd., Sir ARTHUR PORRITT unveiled a model of a proposed "London Varicose Clinic," for the building of which the National Varicose Foundation is appealing to the public for £650,000. The design provides for an out-patient department, 32 ward beds, 8 single rooms, a twin operating suite, a research department, and a lecture hall. The Foundation's chairman, Dr. STANLEY RIVLIN, gave an address on the purposes of the Foundation and showed a film.

Atomic Safety Committee.—Sir DOUGLAS VEALE, until recently registrar at Oxford University, has accepted the chairmanship of a committee set up by the United Kingdom Atomic Energy Authority to advise on training in radiological protection. The committee includes among its members Sir ERNEST ROCK CARLING, Professor W. V. MAYNEORD, and Professor B. W. WINDEYER. The committee will advise the Authority on the training and provision of specialist Health and Safety staff, not only for the Authority's own purposes but also to meet the needs of the nation as a whole.

M.R.C.P.Ed.—At a quarterly meeting of the Royal College of physicians of Edinburgh on May 6 the following were elected members:

J. B. Stanton, J. A. Simpson, K. K. Das, G. Sharan, A. K. Ganguly, J. A. M. Joyce, W. Davison, W. F. K. Morrow, N. S. Capstick, M. Siddique, S. K. Vaish, N. P. Fernando, N. W. J. England, T. O. Ogunlesi, P. E. Goonewardena, N. J. Shah, E. M. Salama, K. Corlett, N. A. E. Samaan, P. J. Koblenzer, N. Berlyne, C. R. Maddock, J. D. Todd, J. Stevenson, G. L. G. Joag, D. J. Patel, I. Ahmad, A. D. Cameron, N. H. Korner, N. B. Sabiel, F. E. Udwadia, A. J. Gazder, M. W. McNicol, S. S. Rikhy, I. Ahmed, P. C. Nag, M. A. Qureshy, D. A. Whiting, B. K. Roy, B. D. Patel.

"Family Doctor" Cookery Book.—*Family Doctor* has issued as one of its periodical publications a cookery and recipe book titled *More Fun with Your Food*. Its slogan is "balanced meals for better feeding." This 60-page illustrated booklet includes recipes for a fortnight of family meals and how to make a "balanced meal" from sandwiches. The price is 1s.

Honorary Degrees at Liverpool.—After the opening of the new building for the Liverpool School of Medicine on May 7 (*Journal*, May 17, p. 1172), the honorary degree of Doctor of Laws was conferred on QUEEN ELIZABETH THE QUEEN MOTHER, Lord ADRIAN, Sir DAVID CAMPBELL, Sir ALLEN DALEY, and Sir JOHN HOBHOUSE, a former Pro-Chancellor of the University and chairman of its development committee.

Mr. V. B. Green-Armytage has been promoted to be an Officer of the Legion of Honour.

COMING EVENTS

Institute of Dermatology.—Semi-permanent exhibition on "Skin Reactions to Fungus Antigens," June 2–30.

British Association of Urological Surgeons.—14th annual meeting, June 19–21 in London. Details from the secretary of the association, 47, Lincoln's Inn Fields, London, W.C.2.

Health Education.—Summer school on "The Science and Art of Health Education," August 19–29 at Bishop Otter College, Chichester. Fee, £22. Details from the Central Council for Health Education, Tavistock House North, Tavistock Square, London, W.C.1.

British Association for the Advancement of Science.—Annual meeting, August 27 to September 3, in Glasgow. Preliminary programmes obtainable from the secretary of the association, Burlington House, Piccadilly, W.1.

European Association Against Poliomyelitis.—The next meeting will be held in Madrid from September 28 to 30. Further information may be obtained from the secretary of the U.K. Committee for Poliomyelitis, c/o The Royal College of Physicians, Pall Mall East, London, S.W.1.

NEW ISSUES

SPECIALIST JOURNALS AND ABSTRACTS

The journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

British Journal of Ophthalmology.—Issued monthly (£6 annually). The new issue, Vol. 42, No. 5, includes:

AMBLYOPIA EX ANOPSIA (SUPPRESSION AMBLYOPIA). S. Mayweg and H. H. Massie.
MODIFIED MAJOR AMBLYOSCOPE. A. Stanworth.
A CONTRIBUTION TO THE EXPERIMENTAL STUDY OF THE ALLERGIC PROCESSES OF THE ANTERIOR SEGMENT OF THE EYE. A. Keckarovski.
STURGE-WEBER'S SYNDROME. Jan Luc.
EXAMINATION OF THE EYE WITH INFRA-RED RADIATION. A. J. Ogg.
SPONTANEOUS HYPHAEMA WITH ABNORMAL IRIS VESSELS. P. U. Fechner.
INSECT STING OF THE LID—AND A SEQUEL. Frank W. Law.

Abstracts of World Medicine.—Issued in the first week of each month, this journal contains abstracts of important papers selected from the current medical literature of the world. Annual subscription £4 4s.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Tuesday, May 27

INSTITUTE OF CHILD HEALTH.—5 p.m., Dr. G. M. Guest (Cincinnati): Studies of Insensible Weight Loss.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. G. C. Wells: Use of Steroids in Dermatology.
●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Hammersmith Hospital, 3 p.m., Professor J. L. Wright (Otago): Anatomy of Prolapse.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. J. K. Oates: Reiter's Disease.
ROYAL STATISTICAL SOCIETY: MEDICAL SECTION.—At Westminster Medical School, 5.30 p.m., annual general meeting. Mr. R. E. Waller: Mortality from Lung Cancer in Relation to Population Density.

Wednesday, May 28

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. T. Brain: Electrotherapeutic Techniques.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. R. Bignall: Course of Carcinoma of the Lung.
●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Queen Charlotte's Hospital, 9.45 a.m., Professor J. L. Wright (Otago): Toxaemia and Eclampsia in New Zealand.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. C. H. Andrewes: Influenza—Asian and Otherwise.

Thursday, May 29

HONYMAN GILLESPIE LECTURE.—At Anatomy Theatre, University New Buildings, Edinburgh, 5 p.m., Professor Ian Aird: Clinical and Operative Surgery of Parathyroid Tumours.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. A. Tickner: Epidermal Proteins.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. Sheila Sherlock: Hepatic Coma.
ROYAL SOCIETY.—4.30 p.m., Group Captain W. K. Stewart: Institute of Aviation Medicine.
ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. Desmond Curran: postgraduate demonstration in psychiatry.

Friday, May 30

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. G. C. Wells: clinical demonstration.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. G. Scadding: clinical demonstration.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—10 a.m., Mr. E. R. Frizelle: Thoughts and Impressions in Gastro-duodenal Surgery.
●ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS.—5 p.m., William Blair-Bell Memorial Lecture by Dr. J. S. Scott: Pregnancy Toxaemia Associated with Hydrops Foetalis, Hydatidiform Mole, and Hydramnios.
ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Institute Theatre, 5 p.m., Mr. C. W. A. Kimbell: Carcinoma Corporis Uteri.

Saturday, May 31

WEST MIDLANDS PHYSICIANS ASSOCIATION.—At Burton-on-Trent General Hospital, 11 a.m., spring meeting.

Sunday, June 1

COLLEGE OF GENERAL PRACTITIONERS: YORKSHIRE FACULTY.—At Royal Bath Hospital, Cornwall Road, Harrogate, 2 p.m., G.P. Symposium on Rheumatism.
UNIVERSITY COLLEGE HOSPITAL.—10.15 a.m., Lecture-demonstration for general practitioners. Clinical demonstration by Dr. W. R. Trotter: Thyroid Diseases.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Hetherington.—On May 15, 1958, to Monica, wife of Dr. A. W. Hetherington, of Redcote, Rainham, Essex, a daughter—Emma Katharine.
Solomon.—On May 11, 1958, at Torbay Hospital, to Dr. Madeleine (formerly Epstein), wife of Dr. Louis Solomon, of "Pleasant," Barcombe Heights, Paignton, Torbay, Devon, a daughter.
Turner.—On May 13, 1958, to Naomi (formerly Myers), M.R.C.S., L.R.C.P., D.C.H., wife of Maxwell H. Turner, M.B., Ch.B., M.M.S.A., of Green Meadows, Middlefield Lane, Hagley, Worcs., a brother for Deborah Celia.

DEATHS

Turner.—On April 29, 1958, at Stoke Mandeville Hospital, Aylesbury, Bucks, Geoffrey Moore Turner, M.R.C.S., L.R.C.P., of Park Farm, Potter Row, Great Missenden, Bucks, aged 45.
Woodside.—On March 10, 1958, at King's Mill Hospital, Sutton-in-Ashfield, Notts, Robert Woodside, L.R.C.P.&S.Ed., L.R.F.P.S., of Healdswood House, Skegby, Notts, aged 67.

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

British and American Vaccine

Q.—*Is development of immunity interfered with when British vaccine is used for the first antipoliomyelitis immunizing injection and American vaccine for the second ?*

A.—The "American" poliovirus vaccine being distributed by local authorities is also made at the Connaught Laboratories, Toronto. Like the British vaccine, it contains all three types of poliomyelitis virus killed by formaldehyde, but the type 1 of the American vaccine is the Mahoney strain, whereas the type 1 of the British vaccine is the Brunhilde (Enders) or "Brunenders" strain ; types 2 and 3 are the same strains in both. There seems to be no significant difference in the protective potency of the two vaccines: two injections of either preparation can protect between 70% and 80% of the subjects. No evidence has been produced, so far as I know, that an injection of the American vaccine given after an injection of British vaccine interferes with the development of immunity against poliomyelitis and there is no *a priori* reason to think that it can. No booster dose nor any special action is called for.

Fuel Oil at the Seaside

Q.—*What is the best way of removing fuel oil from the skin of children contaminated while playing on the beach ?*

A.—The use of petrol to remove fuel oil from the skin is highly dangerous, since, apart from the risk of poisoning and the possibility of subsequent dermatitis, there is also a fire risk.

Simple remedies should be tried first—thorough washing with soap and warm water, using a shower-bath if possible. Ordinary household detergents may succeed where soap fails, although some skins are sensitive to these materials. Oil in the hair may be removed by rubbing in butter or margarine or any bland type of fat such as olive oil. The R.S.P.C.A. use wood flour or fuller's earth for removing the oil from the feathers of contaminated birds, and this should be effective for a child's hair. Oil in the eyes may call for hospital treatment, but bland liquids such as liquid paraffin or castor oil, with a little local analgesic if there is much pain, are probably the most useful immediate treatment. Cleansing creams such as "kerocleanse No. 23" are stated to be very effective in removing oil from the body. They are applied to the contaminated areas and when washed off bring the oil away also.

Gout and Allergy

Q.—*Is there any available evidence to suggest that gout is an allergic disease ?*

A.—The question of whether gout is an allergic disease, or more particularly whether an attack of gout is due to hypersensitivity to an unknown allergen, is as yet unsolved. Lord Cohen, in his chapter on gout in Copeman's *Textbook of Rheumatic Diseases*,[1] finds no evidence that the incidence of other manifestations of the allergic diathesis, such as asthma, urticaria, and angioneurotic oedema, occur with greater frequency in the gouty as compared with the non-gouty. The mechanism of an attack of gout is still unknown, and particularly its relationship to the hyperuricaemia which is present in this disease. Two arguments have been put forward in favour of an allergic element: first, the vascular phenomena which appear locally in an attack suggest increased permeability ; secondly, the therapeutic results achieved by colchicine and phenylbutazone, which are not associated with any rapid alteration in the level of serum uric acid. The possibility has also been raised in an article by Villa, Robecchi, and Ballabio.[2] They state that an allergic basis is suggested by the fact that there is difficulty in interpreting the disease on the basis of a single metabolic alteration ; that there can be an acute attack with a normal uric acid level in the blood or alternatively a high uric acid level throughout life without gouty manifestations ; and that acute gout and anaphylaxis can occur simultaneously. In fact, up to date there is little evidence that gout is an allergic disease, and no specific or non-specific allergens have been implicated by scientific means.

REFERENCES

[1] Cohen, H., in *Textbook of Rheumatic Diseases*, 1955, 2nd ed., edited by W. S. C. Copeman. Edinburgh.
[2] Villa, L., Robecchi, A., and Ballabio, C. B., *Ann. rheum. Dis.*, 1958, **17**, 9.

Bactericidal Properties of Detergents

Q.—*Is "stergene" useful in acne and furunculosis as a bactericidal skin wash ?*

A.—We are informed by the manufacturers of stergene that its active constituent is a non-ionic detergent, and that bactericidal powers are not claimed for it. Non-ionic detergents as a class have little antibacterial activity, and such virtue as they may possess for medical purposes is owing to their surface-active and cleansing properties. The use of stergene for removing crusts from a burned area of skin was recently commended in the correspondence columns of the *Journal*.[1] Its only action on whole skin would be of the same nature, and might be particularly effective if the skin were greasy. Compounds of this class can cause sensitization : repeated use may thus eventually produce a dermatitis.

REFERENCE

[1] Wilson, T. R., *Brit. med. J.*, 1958, **1**, 160.

Cataract and Diabetes

Q.—*Is there any evidence to prove that diabetes can cause cataract of the lens ?*

A.—Yes, but it must be remembered that there are two kinds of cataract which may occur in diabetic subjects. First, ordinary lens changes of the senile type, which, however, occur more frequently and at an earlier age than in non-diabetics and tend to progress more rapidly.[1] Secondly, true diabetic cataract, characterized by widespread and pathognomonic subcapsular changes occurring bilaterally, which tends to run an acute course and occurs preferentially in young persons. The latter type is rare, and is due essentially to osmotic influences. There is abundant experimental proof of the relationship of the lens changes to the diabetic state in this type of cataract.

REFERENCE

[1] Kirby, D. B., *Arch. Ophthal.* (*Chicago*), 1933, **9**, 966.

Disinfection after Scarlet Fever

Q.—*What is the modern practice for terminal disinfection of the patient's room and belongings in a case of scarlet fever ?*

A.—The main source of infection is the patient himself. If he is treated with penicillin either by one long-acting dose or continuously for 10 days he is unlikely, if he is free from discharges, to be infectious thereafter. Crockery can be boiled, comics and the like burned. Pyjamas will be adequately disinfected in the domestic washing machine or sink. Few doctors would bother to disinfect or even wash the blankets in the case of their own children unless the bed was to be occupied at once by someone else. As regards the room, ordinary cleaning, preferably with a vacuum cleaner, and thorough ventilation is all that is necessary. Disinfectant measures, unless applied with scientifically controlled thoroughness, have little effect on pathogens in